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EPIDEMIC *SALMONELLA NEWPORT* INFECTION IN A METROPOLITAN AREA

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SALMONELLA infection in Massachusetts occurs both sporadically and in epidemic form.[1] By and large, most clinical cases are brought to light as a result of cultural studies on patients with gastrointestinal or enteric symptoms. When organisms recovered from patients or carriers are classified according to the Kauffmann–White schema, a large variety of salmonella types is demonstrated.[2,3] However, under ordinary circumstances certain types appear more frequently than others. In Massachusetts, for example, *Salmonella typhimurium* and *S. newport* together accounted for 57.5 per cent of all sporadic cases in a study covering seven years.[1]

S. typhimurium and *S. newport*, although somewhat different in antigenic composition, show certain characteristics that are similar. From the clinical point of view, gastrointestinal symptoms predominate in cases from these species as opposed to *S. paratyphi B*, for example, which is manifested principally by sustained pyrexia. In our experience permanent localization of the organism in the gall bladder rarely occurs after infection with *S. typhimurium*. No permanent *S. newport* carriers could be found in our records or in the literature, whereas about 2 to 4 per cent of patients recovering from *S. paratyphi B* become chronic carriers. Although *S. paratyphi B* is essentially a disease of human beings, *S. typhimurium* and *S. newport* are recovered from human, animal, and avian sources.

It is the purpose of this paper to describe an extensive outbreak of infection due to *S. newport* throughout a large metropolitan area. Analysis of the epidemiology includes demonstration of the source of infection and principal method of transmission. In addition, an attempt is made to compare the frequency of clinical as opposed to subclinical infection among persons exposed to the causative agent.

To keep the rate of secondary infection among the household contacts of patients with primary disease as low as possible, prompt control measures were instituted in co-operation with the several local health departments of the area. Local health officers, public-health nurses, sanitarians and practicing physicians participated in these activities.

Bacteriologic studies were performed at the Diagnostic Laboratory of the Massachusetts Department of Public Health. Isolation of *S. newport* from chopped liver was made within forty-eight hours. At about the same time *S. newport* was isolated from most of the stools submitted at the beginning of the outbreak. For primary isolation the stool specimens were streaked on bismuth sulfite agar, and a portion added to tetrathionate enrichment broth, which was subsequently plated on bismuth sulfite agar.

By and large, clinical diagnosis was based on signs and symptoms, with confirmation by stool culture. To standardize the information obtained with the assistance of the several health departments concerned, a single form was developed upon which clinical as well as epidemiologic data were recorded.

Epidemiology

Verifying the Existence of the Outbreak

On June 3, 1946, several cases of food poisoning in persons residing in two suburban communities were reported to the District Health Officer. All patients had attended 1 of 2 confirmation parties at either Temple K, in community A or Temple E in community B.

Investigation revealed that many persons who attended one or the other of the parties had become ill twelve to thirty hours later. The parties took place at about 12:45 p.m. on June 1, and the food for both parties had been prepared by the same caterer.

Subsequently, it was learned that persons attending a wedding reception on the afternoon of June 2 in a private home in community C had also become ill. Food served at this party had been purchased from the same catering concern.

Gastrointestinal symptoms predominated among those who became ill. For the most part, patients complained of nausea, vomiting, abdominal cramps,

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diarrhea and fever. In some cases continued fever was the outstanding clinical manifestation, and gastrointestinal signs and symptoms were insignificant. There was only 1 death, which occurred in a patient with pre-existing chronic disease.

Investigation of other parties served by the caterer revealed that illness had occurred among persons attending 2 additional parties held on June 2, making a total of 5 gatherings involved.

Tabulation of the cases associated with the whole outbreak showed that, although persons from 27 Massachusetts cities and towns had become ill, about 85 per cent of the patients resided in the Greater Boston area. Illness had occurred in guests from 7 other states and the Dominion of Canada.

Of a total of 1019 persons known to have been present at the five parties (Table 1), clinical and epidemiologic data were obtained from 750, of whom 425 (57 per cent) had become ill. Of these 425 persons the day of onset of illness was determined in 408. A common pattern of time of onset (Fig. 1) can be noted among all 5 parties. The day of onset for all the parties is shown in Table 2. It is apparent that 12 per cent of the patients became ill on the first, 60 per cent on the second, and 21 per cent on the third day. The incubation period was four days or less in 97 per cent of the cases. The possibility of secondary spread among contacts of patients with primary infection cannot be excluded in the single infections occurring on the fifteenth, seventeenth and twentieth days.

The clinical attack rates varied considerably among the several parties (Table 1), ranging from 21 per cent (Party 5) to 83 per cent (Party 1). The over-all attack rate for all 5 parties was 57 per cent. A comparison of the combined attack rates for the parties held on June 1 and June 2 revealed a marked difference, being 73 per cent for the former and 36 per cent for the latter. Statistically, the difference between these rates is significant (Table 1).

The frequency of positive cultures among patients and exposed persons who were not made ill is shown in Table 3. It is apparent, as one would expect, that when the clinical attack rate was high the proportion of exposed persons with positive cultures was also greater, among both the sick and the well. Of 316 cultures, 221, or 70 per cent, were positive for *S. newport*, whereas of 162 well, exposed persons, 42 or 26 per cent, were harboring the etio-

TABLE 1. *Attack Rates in Outbreaks of Infection.*

PARTY No.	DATE	ATTACK RATES FOR 5 PARTIES: NO. OF GUESTS	NO. OF GUESTS STUDIED	NO. ILL	ATTACK RATE	DATE	COMPARISON OF ATTACK RATES (June 1 and June 2 Parties): NO. STUDIED	NO. ILL	ATTACK RATE	STANDARD DEVIATION*
					%				%	
1	June 1	300	235	194	83					
2	June 1	256	180	110	61	June 1 Parties	415	304	73	2.2
3	June 2	75	61	31	51					
4	June 2	165	133	61	46					
5	June 2	223	141	29	21	June 2 Parties	335	121	36	2.6
Totals Average		1019	750	425	57					

*Sigma of difference, 3.4; actual difference, 37 = 10.8 times the sigma of the difference.

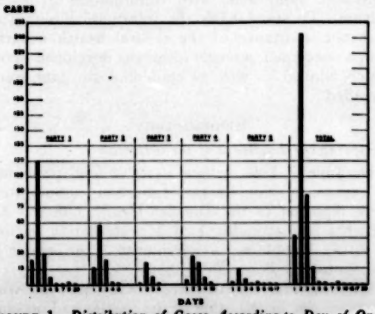

FIGURE 1. *Distribution of Cases According to Day of Onset.*

TABLE 2. *Distribution of Cases by Day of Onset.*

DAY	NUMBER ILL JUNE 1 PARTIES	NUMBER ILL JUNE 2 PARTIES	TOTAL	PERCENTAGE
1	41	7	48	12
2	181	63	244	60
3	54	33	87	21
4	9	8	17	4
5 (or longer) *	6	6	12	3
Totals	291†	117‡	408	

*1 on 5th day, 2 on 6th day, 1 on 7th day, 2 on 9th day and 1 each on 10th, 15th, 17th and 20th days.
†Day of onset not known in 13 cases.
‡Day of onset not known in 4 cases.

logic agent. Of 478 persons sick or well and exposed to the infectious agent, 263 or 55 per cent had positive stool cultures.

Establishing the Source of Infection

Study of the foods served showed that only two items, chopped liver and "knishes," were common to the 2 parties served on June 1. It was learned that one of the cooks, who had eaten sandwiches made from the same batch of chopped liver, had also become ill with salmonella infection. This person had not eaten the "knishes." Analysis of obtained from 4 other food handlers, who had eaten varying amounts of chopped liver before it left the commissary on June 1. These workers gave no history of recent illness before the occurrence of the outbreak.

Discussion

The epidemiologic investigation indicated that an unrecognized case of infection due to *S. newport* was the source of the outbreak. The importance of adequate study of patients with signs and symptoms of gastrointestinal or enteric disease has been

Table 3. *Frequency of Positive Cultures in Clinical and Subclinical Infections.*

Party No.	Clinical Cases		Subclinical Cases		Totals	
	No. of cultures	No. positive	No. of cultures among well persons	No. positive	No. of cultures	No. positive
1	158	126 (80%)	30	13 (43%)	188	139 (74%)
2	76	49 (64%)	36	9 (25%)	112	58 (52%)
3	27	21 (78%)	6	2 (33%)	33	23 (70%)
4	46	22 (48%)	42	12 (29%)	88	34 (39%)
5	9	3 (33%)	48	6 (13%)	57	9 (16%)
Totals ..	316	221 (70%)	162	42 (26%)	478	263 (55%)

check lists of foods, completed by infected and noninfected guests, revealed a high degree of correlation between illness and partaking of chopped liver. Cultures of chopped liver available among unconsumed items left over from 2 of the parties were positive for *S. newport*.

The chopped liver served on June 1 had been prepared during the morning of May 31, the preparation having been completed about noontime. It was taken to Temple K during the afternoon of May 31, where it was placed in a refrigerator until it was served on June 1. The portion of liver intended for Temple E was refrigerated in the caterer's commissary until the morning of June 1, when it was transported to Temple E, where the food was kept at room temperature from 9 a.m. until it was served. The chopped liver served on June 2 was prepared during the night of June 1. After preparation it was put into two pans. To one pan was added about 1½ pounds of chopped liver left over from the batch made on May 31.

Both batches of liver had been prepared largely by E. L., one of 21 food handlers employed by the caterer. This thirty-four-year-old female worker had become ill on May 18 with complaints of abdominal pain, diarrhea and fever. She was treated by her physician, remaining home from work for several days until, upon his advice, she returned on May 27. No stool cultures were taken during her illness.

Stool cultures of E. L., taken during the course of the investigation, were consistently positive for *S. newport*. Positive stool cultures were also emphasized in a previous communication.[1] Failure to establish an etiologic diagnosis in such cases may result in the transmission of infection by food handlers to contacts in the home or throughout the community. Hospital and public-health laboratories are prepared to culture specimens from such patients at the request of practicing physicians. Analysis of cultures submitted by physicians to public-health laboratories reveals that specimens are usually submitted by the same group of physicians interested in establishing etiologic diagnosis in cases of food poisoning.

It has been shown that bacteriologic study of contacts to patients with salmonella infection will disclose a certain number of secondary cases, as well as a substantial amount of subclinical infection. Demonstration of these infections aids in the control by breaking chains of spread.

The primary purpose of the administrative procedures instituted to control this outbreak was aimed at reducing the rate of spread among contacts of the primary cases to the lowest possible point. This result was accomplished by prompt reporting of patients and exposed persons to local health departments and by the immediate supervisory measures established by such agencies. Of a sample of 206 household contacts of persons infected at the parties, who were studied clinically and by laboratory examinations, only 13 secondary infections were demonstrated. Of these, 9 were subclinical cases, and only 4 had clinical signs or symptoms of infection due to *S. newport*.

In view of the large number of secondary infections that occur under normal circumstances and the few secondary cases demonstrated in this situation, the value of prompt follow-up study of salmonella infections by local health departments becomes apparent. The relatively high proportion of subclinical infection demonstrated by the study suggests the need of examining all exposed contacts, sick or well, for the presence of infection.

The combined attack rate for the June 1 parties was significantly greater than that of the June 2 parties (Table 1). The liver remaining from batch A was apparently not mixed with batch B until the morning of June 2. This factor may account for the lower attack rates for the parties served on June 2.

Subsequent examination of patients with positive stool cultures revealed no permanent gall-bladder carriers. Apparently *S. newport* does not tend to localize in the gall bladder as some other species of salmonella do. This finding is consistent with previous studies,[1] in which it has been shown that prolonged follow-up examination of human cases of infection with *S. newport* does not reveal chronic gall-bladder carriers.

Summary

In an outbreak of infection due to *Salmonella newport*, 1019 persons were exposed to contaminated chopped liver in 5 different parties served on two successive days by the same caterer. Of 750 persons investigated, 425, or 57 per cent, became ill.

Of 478 persons examined cultures were positive in 263, or 55 per cent. The rate of positive cultures was 70 per cent among clinical cases and 26 per cent among persons who were not ill.

The incubation period was as follows: 72 per cent of the patients became ill in forty-eight hours, whereas 97 per cent had their onset four days or less after exposure.

Epidemiologic investigation revealed, as the source of infection, a food handler who was an unrecognized convalescent carrier of *S. newport*. Before investigation of the outbreak, no attempt had been made to establish an etiologic diagnosis of this food handler's gastrointestinal illness before she was allowed to return to work.

The importance of establishing a diagnosis in cases of gastrointestinal or enteric disease, particularly in food handlers, is emphasized.

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GLOMERULONEPHRITIS AS A COMPLICATION OF THE SCHÖNLEIN — HENOCH SYNDROME*

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RENAL bleeding, either gross or microscopic, is a fairly frequent manifestation of the Schönlein–Henoch syndrome. Usually, it is ascribed to the increased capillary permeability that is one of the features of this illness. However, in 1852, Johnson[1] noted the association of purpura with renal disease and albuminuria. Since then, the occurrence of glomerulonephritis as a visceral complication along with or in the wake of allergic purpura, erythema or edema has been a controversial issue. In 1899 Henoch[2] referred to nephritis as a frequent complication of the syndrome and reported 3 such cases. Osler,[3, 4] Pratt[5] and Lippman[6] described classic glomerulonephritis in a number of their patients. Macalister[7] was so impressed with the frequent association that he considered Schönlein–Henoch purpura to be a variety of Bright's disease. Zothe[8] described 2 patients, 1 of whom died with classic chronic glomerulonephritis. However, Christian[9] took issue with this concept, believing that the renal lesions were due to the same process as that in the skin.

Because of the usually benign nature of this syndrome, relatively few pathological studies have been recorded. These include widespread focal glomerulonephritis of the type found in subacute bacterial endocarditis,[10] tubular atrophy and rarefaction of the malpighian corpuscles[11] and nephrotic kidneys.[12] Watson[13] reported a case with autopsy findings of classic glomerulonephritis. In a study of 12 cases of the syndrome Gairdner[14] reported 5 with glomerulonephritis. In 1 case subacute glomerulonephritis was found at autopsy; of particular interest was the finding of cerebral necrotizing arteriolitis. Similar arterial lesions were produced experimentally in animals by Gruber[15] as a manifestation of hypersensitivity to foreign serum. This work has been confirmed by many others, some of whom also produced glomerulonephritic lesions.[16-19]

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Our interest in this subject was provoked three years ago when the opportunity to observe and study 2 patients with glomerulonephritis associated with the Schönlein–Henoch syndrome presented itself. While recovering from the purpuric manifestations 1 patient died of a pneumonic spread of an unrelated pulmonary tuberculosis. The kidneys became available for a pathological study.[20] During the past three years we have observed 3 more cases of this syndrome, with autopsy study in another case. This case demonstrated arterial lesions similar to those reported by Gairdner.[14]

Case Reports

Case 1. A 23-year-old woman was admitted to the hospital in April, 1952. The chief complaint was bloody diarrhea. The present illness had started 1 month before, when she suffered from an upper respiratory infection manifested by coryza and sore throat. She was treated with penicillin and "empirin" compound. The symptoms abated but returned 1 week later in milder form. One week before admission, swelling of the face and ankles was noted for the first time. Two days later nausea, vomiting and diarrhea, with tarry and bloody stools, developed.

There was no history of allergy, previous renal or gastrointestinal disease or scarlet fever. She had been hospitalized 2 years before for maternity care, and no evidence of renal disease or hypertension had been found. Her parents and siblings were living and well. Review of systems was negative.

Physical examination revealed a well nourished and well developed woman in no acute distress. There was a papillary rash in the right axilla. A small, tender lymph node was palpated in the left cervical region. Slight epigastric tenderness was elicited on deep palpation. Examination of the ocular fundi, lungs, heart and extremities was not remarkable. The remainder of the physical examination was within normal limits.

The temperature was 99.8°F., and the pulse 82. The blood pressure was 140/88.

Examination of the blood showed a hemoglobin of 14.0 gm. per 100 cc. and a white-cell count of 15,000, with 64 per cent neutrophils, 35 per cent lymphocytes and 1 per cent monocytes. An adequate quantity of platelets were seen on routine blood smear. The sedimentation rate was 20 mm. in 1 hour. The Mazzini test was negative. The blood urea nitrogen was 48 mg. per 100 cc. The phenolsulfonephthalein elimination was 44 per cent in 2 hours. The specific gravity of the urine was normal, and there was a moderate amount of albumin, with many red blood cells, 10 to 20 white blood cells and 3 to 5 granular casts per high-power field in the sediment. Tests for occult blood in the stools were positive.

On bed rest the patient recovered uneventfully. The blood pressure dropped to 110/80; the phenolsulfonephthalein elimination was normal 1 month after admission. The blood urea nitrogen dropped to normal levels 5 days after admission. At the time of discharge a persistent microscopic hematuria, with 2 to 10 red blood cells per high-power field in the sediment, was still present.

Case 2. A 24-year-old man was admitted to the hospital in May, 1952. The present illness had started 5 weeks previously as an upper respiratory infection with a sore throat for which penicillin had been administered intramuscularly. There was a remission of symptoms for 1 week, when the sore throat returned, with a temperature of 102°F. Again he was treated with penicillin, both intramuscularly and orally. The sore throat abated but recurred 5 days later and was associated with aching of the extremities. At this time he was admitted to another hospital. Shortly after this admission he noted swelling and redness of the hands and forearms and pain in the small joints of the hands. There was also "weakness" of the left arm and hand. The erythema, swelling, arthralgia and weakness gradually disappeared over a 2-week period, when he signed himself out of the hospital.

The past history indicated that he had never been seriously ill. There was no history of allergy. He had been discharged from the Army in June, 1951, in good health. The family history was noncontributory.

Physical examination disclosed a Grade 2 apical systolic murmur, an ecchymotic area over the left deltoid muscle, tenderness of the left biceps and triceps muscles, weakness of the grip on the left and small, nontender, soft, palpable lymph nodes in the submandibular and posterior cervical regions. The blood pressure was 135/92.

Examination of the blood revealed a white-cell count of 16,000, with 66 per cent neutrophils and 34 per cent lymphocytes; a subsequent count was 9000, with 50 per cent neutrophils, 47 per cent lymphocytes and 3 per cent eosinophils.

Table 1. *Hematologic Data in Case 4.*

Date	Red-Cell Count	Hemoglobin	Platelets	White-Cell Count	Blood Urea Nitrogen	Creatinine
1949	*$\times 10^6$*	*gm./100 cc.*	*$\times 10^3$*	*$\times 10^3$*	*mg./100 cc.*	*mg./100 cc.*
June 17	4.80	14.0	280	31	—	—
July 13	3.70	10.0	—	22	88	2.4
14*	3.30	9.0	—	—	—	—
15	3.77	11.0	220	37	100	—
18*	1.73	5.5	—	21	—	—
19*	2.68	6.0	—	18	—	—
20*	2.89	7.0	—	9	—	—
21*	4.0	10.8	—	—	85	7.0
22*	—	—	—	—	80	—

*500-cc. transfusions given on these dates.

The sedimentation rate was normal, as were the red-cell count, hemoglobin and platelet count. Daily urinalyses showed strong traces of albumin, with many red blood cells and 5 to 30 white blood cells per high-power field and occasional granular casts in the sediment. The quantitative urinary albumin fluctuated in the range of 0.180 to 0.240 gm. per 100 cc. in 24 hours. The urea clearance was 67 per cent of the average normal clearance. A phenosulfonephthalein test disclosed that 47 per cent of the dye was eliminated. A biopsy of the left deltoid muscle revealed no abnormality. Urea nitrogen determinations were repeatedly normal. An intravenous pyelogram was normal, as were all other studies performed, including examination of the spinal fluid, antistreptolysin titer, heterophil-antibody agglutination, trichinella precipitin test, bleeding, coagulation and prothrombin times, an electrocardiogram and x-ray films of the chest, dorsal spine, left shoulder and arm.

During his hospital stay the patient was comfortable and did not offer any complaints. He was discharged, with persistent albuminuria and microscopic hematuria, to the care of his private physician.

Case 3.* A 50-year-old man was admitted to the hospital in August, 1949. The chief complaints were vomiting and abdominal pain. The present illness had started in the last week of July with a generalized dermatitis due to poison ivy. The rash persisted during the first 2 weeks of August. On

*Previously reported by Levitt et al.[20] and included here with the permission of the publisher.

August 10 he received the last of a series of 6 injections of Ivyol. Approximately 1 week later, painful swelling of the joints was noted. This was soon followed by persistent vomiting, abdominal cramps and bloody diarrhea. The stools became tarry. The patient then became constipated, requiring enemas or cathartics. Ten days before admission, a "pink rash" appeared on both feet, followed in 24 hours by generalized urticaria, pruritus and fever. A few days later, bright-red spots were noted on the lower extremities. He received glucose parenterally and "allergy"

FIGURE 1. *Microscopical Section of a Kidney (Low-Power) in Case 4, Showing Glomerulonephritis (Reproduced from Levitt et al.,[20] with the Permission of the Publisher).*

pills. He also had received sulfonamides and penicillin after the rash appeared.

According to the past history, he had had hives in 1945 after sulfonamide medication. Otherwise he had never been seriously ill. A military induction examination in 1942 and the discharge examination in 1946 had not revealed any hypertension, albuminuria or hematuria. Previous insurance examinations were also negative for renocardiovascular disease. His mother had died at the age of 68 of a cerebral hemorrhage. The family history was otherwise noncontributory. Review of the systems was negative.

Physical examination demonstrated a well nourished and well developed man in no acute distress. There was no adenopathy. The conjunctivas were somewhat pallid. Examination of the lungs, heart and abdomen was not remarkable. Numerous petechiae were scattered over the lower portion of both legs. Many brownish macules, thought to be fading purpuric areas, were noted over the lower extremities. The remainder of the examination was within normal limits.

The temperature was normal and the pulse 106. The blood pressure was 172/108.

Examination of the blood showed a red-cell count of 3,840,000, with a hemoglobin of 11.4 gm. per 100 cc., and a white-cell count of 9450, with 84 per cent neutrophils, 2 per cent stab forms and 14 per cent lymphocytes. The platelet count was 550,000. The sedimentation rate was 25 mm. in 1 hour. Bleeding, clot retraction, coagulation and prothrombin times were normal. A blood serologic test was negative. The blood urea nitrogen was 21.4 mg. per 100 cc. Urea clearance and phenolsulfonephthalein kidney-function tests were negative. The urine had a normal specific gravity and contained a trace of albumin, with 3 to 7 red blood cells per high-power field in the sediment. A +++ test for occult blood was found in the stools. Sternal-marrow aspiration revealed normoblastic hyperplasia with an increase in eosinophils.

On bed rest, antihistaminics, calcium gluconate and ascorbic acid therapy, the patient made an uneventful recovery. The blood pressure dropped to 140/96. However, a few red blood cells persisted in the urinary sediment up to the time of discharge.

FIGURE 2. *Microscopical Section of a Kidney (High Power) in Case 4, Showing Reduplication of Bowman's Capsule, Adhesions, Exudation, Swelling and Tufting (Reproduced from Levitt et al.,[20] with the Permission of the Publisher).*

CASE 4.* A 58-year-old man was admitted to the hospital in March, 1947, with bilateral pulmonary tuberculosis. He was treated conservatively throughout his hospital stay. The history and repeated routine urine and blood chemical examinations were negative for renal disease. There was no indication of previous allergic manifestations. The course was uneventful until June 9, 1949, when acute sinusitis and pharyngitis occurred. A throat culture was positive for nonhemolytic streptococci and *Staphylococcus aureus*. On June 15 300,000 units of penicillin in beeswax and oil was injected

*Previously reported by Levitt et al.[20] and included here with the permission of the publisher.

intramuscularly. On June 17 a papular rash appeared on the hands and face. Antihistaminic drugs were given. The patient slowly improved until June 25, when purpuric spots were noted on the cheeks, buttocks and all extremities. On June 27 gross hematuria and pain and swelling of the elbows, wrists, ankles and metacarpalphalangeal joints were the predominating features. The pharyngeal mucosa was hemorrhagic. On this date the white-cell count was 31,800, with 91 per cent neutrophils and 9 per cent lymphocytes; the hemoglobin was 14 gm. per 100 cc., the sedimentation rate 23 mm. in 1 hour, the platelets 280,000, and the prothrombin time 89 per cent of normal. The fragility of the red blood cells and bleeding and clotting times were normal. The results of blood counts throughout the course are presented in Table 1. Bone-marrow aspiration disclosed mild normoblastic hyperplasia; the megakaryocytes were normal. Throughout this period the patient did not appear to be severely ill.

On July 2 his condition suddenly became critical. The abdomen became greatly distended, and he vomited large quantities of reddish-brown fluid. Gross hematuria persisted. The purpuric lesions became larger and so distended with blood that great hemorrhagic bullae were formed. The joint swelling became massive. The ileus was treated with Wangensteen suction and parenteral infusion of fluids. Large doses of vitamin K, ascorbic acid and antihistaminic drugs were administered. In spite of intensive therapy, this course persisted until exsanguination became so prominent that daily transfusions were required. Nitrogen retention was also an outstanding feature at this time. After July 15 the symptoms and signs began to abate and the patient seemed well on the road to recovery. The hematuria and melena disappeared, and the purpuric and bullous skin lesions showed steady resolution. When the gross hematuria disappeared, albuminuria and microscopic hematuria were persistent findings.

On July 22 the temperature rose suddenly to 101°F., the pulse to 130, and the respirations to 32. Examination disclosed diffuse subcrepitant rales throughout both lung fields. This was interpreted as an acute caseating bronchopneumonia. In spite of intensive therapy the patient died on July 23.

Autopsy was performed 5 hours after death, which was found to have been caused by extensive caseating tuberculous bronchopneumonia throughout both lower-lung fields. Grossly, the gastrointestinal tract was normal except for the proximal end of the jejunum, where there was a 5-cm. area of raised, firm lesions with slightly ulcerated bases, each of which measured approximately 0.5 cm. in diameter and was irregularly placed around the mucosa. The lesions were soft and friable and tended to be pedunculated. No other bleeding points were found. The kidneys were slightly enlarged but normal in position. The cut section showed a well demarcated cortex and medulla, with the cortex averaging 8 to 10 mm. in width. The capsule stripped with a slight amount of difficulty, and the external surface was slightly granular. There were no scars. Both pelves were clear. There were no hemorrhages. The ureters appeared normal. The bone marrow was normal. The skin over the buttocks, lower extremities, upper extremities, abdomen and part of the neck had numerous eschars, measuring 1 to 4 cm. in diameter and with irregular outlines. In some places over the abdomen, petechial-like subcutaneous hemorrhages were seen. There was inflammation around the lesions. No bullae were present. None of these lesions appeared recent.

Microscopical examination of the kidneys (Fig. 1 and 2) showed the capsule to be straight and thin. A small, subcapsular, web-shaped arteriosclerotic scar was present. There was no diffuse increase in interstitial fibrous tissue. The proximal convoluted tubules demonstrated severe swelling, degeneration, vacuolation of the cells and dilatation of the lumen. Some hyaline-cast formation and many areas of fresh red blood cells were present in the tubular lumens. The collecting tubules were empty. The glomerular tufts disclosed increased cellularity. There was a definite reduplication of Bowman's capsule, with crescent formation and fusion to the tufts. No collections of polymorphonuclear leukocytes were seen near the glomeruli. Microscopical section of the skin of a purpuric area revealed normal squamous epithelium except over one small section, where flattening, thinning and loss of papillae occurred. In the corium there were collections of fresh red blood cells, which appeared to fill dilated lumens of endothelium-lined channels. Numerous red cells were found extraluminally in the fibrous connective tissue.

TABLE 2. *Hematologic Data in Case 5.*

DATE	RED-CELL COUNT	HEMOGLOBIN	PLATELETS	WHITE-CELL COUNT	BLOOD UREA NITROGEN	CREATININE
1951	*$\times 10^6$*	*gm./100 cc.*	*$\times 10^3$*	*$\times 10^3$*	*mg./100 cc.*	*mg./100 cc.*
April 9	3.88	12.0	—	15.0	85.0	4.2
10	2.93	9.4	130	16.25	—	—
11	—	—	—	—	104.5	4.7
13	—	—	—	—	111.5	5.0
16	—	—	—	—	153.0	6.2
19*	1.21	4.3	—	14.4	154.0	6.2
20	—	3.5	—	9.2	—	—
21	2.10	8.0	—	7.4	178.0	7.4
23	2.68	8.5	—	7.0	—	—
24	3.06	8.2	—	7.9	—	—
27†	2.80	6.3	—	10.4	200.0	10.8
May 1†	—	—	—	—	136.0	9.7
2	2.50	7.5	—	20.6	100.0	7.6
4†	1.37	5.8	—	13.3	—	—
5†	1.30	6.7	—	7.8	—	—
7†	1.87	7.4	—	9.8	101.0	9.5
8‡	2.50	7.4	—	10.5	96.0	9.5
10	2.20	5.0	—	7.7	113.0	6.5
12	2.60	4.0	—	5.8	—	—
14§	1.47	7.0	—	9.8	—	—
17	3.20	4.8	—	15.2	—	—
18†	2.01	6.6	—	6.5	153.0	13.9
22†	1.98	6.0	—	22.7	134.0	7.3
25	1.96	—	—	31.0	138.0	7.0
26‡	—	—	—	—	—	—

*Two 500-cc. transfusions on this date.
†One 500-cc. transfusion on this date.
‡250 packed red cells given on this date.
§500 packed red cells given on this date.

CASE 5. A 14-year-old Puerto Rican boy was admitted to the hospital in April, 1951. The chief complaint was vomiting. The present illness started during the last week of March, when hives over the arms and face and a petechial rash over the chest, arms, back and face followed the ingestion of strawberries. Several days later, he complained of a sore throat. One week before admission, malaise and small raised areas over the back of the neck developed, and swollen lymph nodes were noted in the neck. Three days before admission there were frequent nosebleeds, and 2 days later he became nauseated and vomited coffee-grounds

material. At that time a stool was black, and the urine was unusually dark.

The past history was noncontributory, and there had not been any allergic manifestations. Both parents were living and well; neither had a history of allergy. The patient was an only child. Review of the systems was negative.

Physical examination showed an acutely ill boy. The face appeared puffy. There was a petechial eruption over the chest, abdomen, back, face, arms, conjunctivas and hard and soft palates. The pharynx was moderately hyperemic. There were large, tender anterior cervical lymph nodes.

FIGURE 3. *Microscopical Section of the Heart in Case 5 (X187).*

An intramyocardial arteriole shows considerable thickening of its wall and obliteration of its lumen. The wall demonstrates fibroblastic proliferation and a few minute deposits of fibrinoid material.

Examination of the heart, lungs and abdomen was not remarkable. The remainder of the examination was within normal limits.

The temperature was 100°F., and the pulse 88. The blood pressure was 136/70.

The patient was azotemic and anemic from the time of admission. Purpura developed over the face and lower extremities. He had numerous nosebleeds, vomiting spells and generalized convulsions. The diastolic blood pressure gradually rose to 110. On May 12 marked retinal edema with numerous punctate hemorrhages, was seen. At approximately the same time a diffuse myalgia and arthralgia developed. On May 18 a gallop rhythm was found and cardiac decompensation was noted. A low-grade fever was present from the 25th day of hospitalization to the time of death. He was treated with supportive measures, including transfusions, digitalis, multivitamins, penicillin and streptomycin and repeated peritoneal lavages, in an attempt to tide him over the azotemia. All treatment was in vain, and he died on the 51st hospital day.

The blood counts, urea nitrogen and creatinine determinations are presented in Table 2. On lumbar puncture, the spinal-fluid pressure was normal, and the fluid was clear. There were 4 lymphocytes per cubic millimeter, a protein of 22 mg., a chloride of 775 mg., and a sugar of 83 mg. per 100 cc. Sickling and lupus preparations were negative, as were agglutination tests for Weil's disease, typhoid O and H, paratyphoid A and B and *Proteus X-19*. Numerous aerobic and anaerobic blood cultures failed to reveal growth. Trichinella precipitin and complement-fixation tests were negative, as were repeat heterophil-antibody tests. A biopsy from the gastrocnemius muscle was normal. Stools were repeatedly negative for ova and parasites. X-ray study of the chest on May 21 demonstrated generalized cardiac enlargement and pulmonary edema. An electrocardiogram was normal on admission; on May 12 there were negative T waves in Leads I, V_4 and V_6; these changes persisted to the end. Sedimentation rates fluctuated between 63 and 88 mm. per hour. The blood sugar varied between 132 and 165 mg. per 100 cc. The bleeding time was 2 minutes and 15 seconds; the clotting time was 4 minutes on one occasion and 6 minutes on another. The fragility of the red blood cells was normal. The Kolmer and Mazzini tests were negative. The total protein was 8.4 gm., with an albumin of 4.5 gm. and globulin

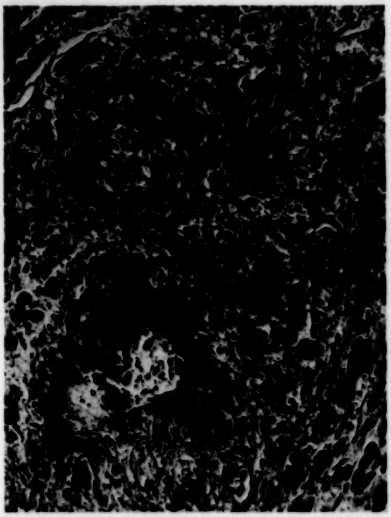

FIGURE 4. *Microscopical Section of the Adrenal Cortex in Case 5 (X150).*

There are small arteries, which show fibrinoid necrosis of their walls. The lumens are distorted and obliterated, and the walls reveal fibroblastic proliferation and accumulations of histiocytes and neutrophils.

of 3.9 gm. per 100 cc. On admission, the cholesterol, cholesterol esters, serum sodium and potassium were within normal limits. The cephalin flocculation test was negative.

Numerous examinations of the urine showed a specific gravity of 1.010 to 1.018, marked albuminuria and numerous red and white blood cells and hyaline and granular casts per high-power field in the sediment.

At autopsy, the positive findings were bilateral, subconjunctival hemorrhages, marked enlargement of the heart (weight, 370 gm.), bilateral hemorrhagic pneumonia and splenomegaly. Each kidney weighed 150 gm. The capsule stripped with difficulty, disclosing a pale, pink external corti-

cal surface with mottled purplish areas. On section, the cut surfaces appeared paler than usual.

On microscopical examination of the heart the arterioles and venules for the most part exhibited fibrous thickening of the intima and partial occlusion of the lumens (Fig. 3). Some vessels contained partially organized, brightly acidophilic fibrinoid material in their lumens. The myocardium of the right and left ventricles contained numerous, small, patchy, focal areas of recent necrosis as well as atrophy and replacement fibrosis of myocardial fibers.

In the lungs the alveolar spaces contained brightly acidophilic aggregates of fibrin and numerous erythrocytes and few neutrophils. The exudate had a hemorrhagic appearance.

There was an increase in the content of hemosiderin in the red pulp in the spleen.

There were small scattered foci of necrosis and neutrophilic infiltration in various portions of the hepatic lobules.

In the adrenal glands (Fig. 4) several small blood vessels, presumably small arteries and arterioles in the cortex, had

FIGURE 5. *Microscopical Section of a Kidney in Case 5 (X150).*

There are two small arteries. One shows a lumen that is narrow but contains erythrocytes; in this vessel there is fibrous intimal thickening. The other vessel demonstrates destruction of its wall, with fibrinoid necrosis. The lumen is occluded.

fibrinoid necrosis in their walls and partial or complete occlusion of their lumens. There was adventitial fibroblastic proliferation, with small numbers of neutrophils and eosinophils. One portion of cortex showed a small focus of necrosis and neutrophilic infiltration.

In the kidneys (Fig. 5 and 6) almost all the glomerular tufts appeared poorly vascularized and partially replaced by fibrous tissue. Bowman's space in places contained erythrocytes, as well as deposits of hemosiderin that were seen principally within the lumens of the cortical and medullary tubules. The interlobular and arcuate arteries as well as other arterioles in the cortex frequently showed considerable fibrous thickening of their intima, with narrowed lumens. In some of the vessels there was fibrinoid change in the intima and neutrophilic and lymphocytic infiltration of the walls. Scattered areas in the renal cortex exhibited recent necrosis of the tubules and glomeruli. These areas of infarction were infiltrated with neutrophils. Most of the cortical tubules had varying degrees of epithelial atrophy and frequently were

FIGURE 6. *Microscopical Section of a Kidney in Case 5 (X100).*

A glomerulus shows marked dilatation of Bowman's space. The lumen of this and of adjoining tubules contains numerous erythrocytes. There is partial fibrosis of glomerular tufts and atrophy of tubules, with a slight, diffuse increase in interstitial fibrous tissue.

separated by increased amounts of interstitial fibrous tissue, which was sometimes infiltrated with numerous lymphocytes.

The final microscopical diagnoses were as follows: subacute glomerulonephritis; generalized arteriolitis, with healed and recent lesions in the adrenal glands, kidneys and heart; focal necrosis and ischemic fibrosis of the myocardium; hemorrhagic, bilateral bronchopneumonia; focal necrosis of the liver; recent infarcts of the kidneys; and focal necrosis of the adrenal cortex.

DISCUSSION

Most observers are agreed that the Schönlein-Henoch syndrome represents an allergic response to a wide variety of antigens. In common with the vast majority of allergic states, it is usually a reversible, transient and benign disability. Pathologically, there is increased capillary permeability, with either exudation of blood (producing purpura

or visceral hemorrhage) or exudation of plasma (causing urticaria or edema of the involved viscera). Thus, in the uncomplicated case, the prognosis is good since there is usually complete recovery from the immediate episode and a return of a normal capillary tone. Although it is difficult to believe that an essentially reversible pathologic reaction can produce an irreversible and progressive lesion such as glomerulonephritis, such a chain of events has been demonstrated in animal experiments.

The group of cases described above present clinical or pathological evidence, or both, of glomerulonephritis occurring in the syndrome. The probable antigens include penicillin, salicylates, Ivyol and a food (strawberries). In 3 cases there appeared to be clinical recovery. This suggests that the renal lesions consisted of the usual reversible pathologic lesions found in most allergic states. However, even in these apparently benign cases, a mild microscopic hematuria has persisted for the several months during which these patients have been observed. In addition, in Case 4, the patient had made a satisfactory clinical recovery from his renal complications, only to succumb to pulmonary tuberculosis. Autopsy, performed two weeks after abatement of the renal condition, disclosed well established and apparently irreversible subacute glomerulonephritis.

Case 5 presented the most interesting sequence of lesions. As far as can be determined a previously healthy youngster developed fulminating glomerulonephritis shortly after a classic episode of Schönlein–Henoch syndrome. This was confirmed by autopsy, which demonstrated a fairly widespread arterial lesion, in part fulfilling the criteria of lupus erythematosus, and in part resembling the lesions of polyarteritis nodosa. Although it is conceivable that Schönlein–Henoch syndrome and glomerulonephritis, or in this case widespread arteritis, might occur simultaneously, Gairdner's[14] description of a similar case with similar renal and extrarenal arterial lesions strongly suggests that these lesions resulted from an allergic reaction. These cases appear to be clinical confirmations of the experimental observations of Gruber,[15] Masugi and Sato,[16] Selye and Pentz,[17] Rich and Gregory[18] and Hawn and Janeway.[19]

Summary

Five cases of glomerulonephritis in association with or in the wake of the Schönlein–Henoch syndrome are described. In all, there is strong evidence that there had not been any pre-existing renal disease.

In 3 cases there was only clinical evidence of the renal lesions. The nephritic condition appeared to be quite benign, but all patients had persistent, mild, microscopic hematuria.

In the 2 fatal cases well established glomerulonephritis was present. In 1, in addition to the renal lesion, there was a widespread arterial lesion, similar to that produced by an antigen-antibody reaction in laboratory animals by numerous investigators.

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MULTIPLE ANTIBODY FORMATION IN AUTOIMMUNE HEMOLYTIC ANEMIA

Report of a Case

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THE precise role of hemolysins in acquired hemolytic anemia has yet to be determined. In 1908 the discovery of these immune bodies in cases of obscure hemolytic anemia by Chauffard and Troisier[1] and by Widal, Abrami and Brulé[2] indicated that a new entity had been found, appropriately called "hemolysinic" anemia. For a number of years these concepts appeared to have been forgotten, and it was not until 1937, when Dameshek and Schwartz[3] demonstrated hemolysins in 2 of 3 cases of acute hemolytic anemia, that a revival of interest took place. The work of these authors re-emphasized the importance of hemolysins, their immunologic nature and their dependence on complement. Nevertheless, the various recent technical advances in the field of immunohematology have greatly favored the discovery of types of immune bodies other than hemolysins in acquired hemolytic anemia. Thus, the use of the Coombs[4, 5] technic revealed the presence of red-cell "coating" antibodies, and trypsinization of test cells[6, 7] and the use of bovine albumin mediums[8, 9] uncovered the existence of circulating serum agglutinins of an "incomplete" or univalent type. Usually, the search for hemolysins, even in cases in which other immune antibodies were present, was completely unrevealing. More recent advances in laboratory technics, however, have enhanced the possibility of detecting hemolysins. Acidification of the test serums as proposed by Gardner and Harris[10] and by Dacie[11] has been of further aid in the demonstration of hemolysins. Most recently, Dacie and de Gruchy[12] have demonstrated that hemolysins may be detected by means of test cells that are either artificially modified by the action of trypsin before use or already abnormal — for example, the red cells from patients with paroxysmal nocturnal hemoglobinuria. Even with these refinements, the detection of hemolysins is quite difficult and far more uncommon than that of "coating" antibodies or agglutinins.

The literature now contains many reports on the beneficial effects of ACTH (adrenocorticotrophic hormone) and cortisone upon autoimmune hemolytic anemia.[13-18] In these reports the authors have usually dwelt on the effect of therapy upon antibodies classified as "coating" antibodies or incomplete agglutinins, although Gardner et al.[18] described the disappearance of "fixed" hemolysins with hormonal therapy in 20 cases. The following case is reported because of the presence of multiple types of antibodies, which responded to cortisone therapy in different fashions.

CASE REPORT

P. E. (N.E.C.H. 58-517), a 33-year-old housewife, was admitted to the hospital on April 17, 1951, with the complaints of increasing pallor and weakness. She stated that she had been "pale" all her life. In 1942, after the birth of her only child, she began to suffer attacks of sciatica radiating down both thighs, and recurring every spring. In 1946 she noted excessive fatigue and was said to have a "low blood count." Parenteral treatment with liver extract was followed by some improvement, and she was in fairly good health until October, 1950, when she noted fatigue and pallor, which gradually increased. In February, 1951, pain in the fingers, wrists, arms, forearms, shoulders and back of the neck, together with slight swelling of the thumbs, wrists and fingers, developed. Pallor became more apparent, and several syncopal attacks occurred. On April 8 she was finally admitted to another hospital, where she received 2 transfusions, and was discharged after 1 week's stay. She was running a low-grade fever and complained of nausea, tinnitus, palpitations and weakness. The urine was dark orange, and icterus was said to be present for a few days before admission.

There was no history suggestive of pleuritis, pericarditis or skin rash. For many years the patient had suffered from seasonal hay fever, occurring mainly in the spring, and had been treated with numerous antihistaminic preparations. The family history was noncontributory.

Physical examination showed a well developed, somewhat thin woman who was extremely pale and slightly icteric. Despite her obvious anemia and a temperature of 104°F. she was not dyspneic and did not regard herself as very ill. The conjunctivas were extremely pale, and the scleras slightly icteric. Small, barely palpable lymph nodes were present in the occipital, axillary and inguinal regions. The chest was clear to percussion and auscultation. The heart was normal in size, the apical impulse being located at the midclavicular line in the 5th interspace. No murmurs were present. There was a sinus tachycardia, with a rate of 120 per minute. Abdominal examination revealed a barely palpable liver and spleen on extreme deep inspiration. No other palpable viscera were noted. No swelling or deformity of the joints was present. There was no eruption of the skin.

Examination of the blood disclosed a red-cell count of 1,040,000, with a hemoglobin of 3.4 gm. per 100 cc. (23 per cent), hematocrit of 13 per cent, reticulocytes of 17.2 per cent and a platelet count of 432,640. The total white-cell count was 13,000, with 57 per cent neutrophils, 31 per cent lymphocytes, 11 per cent monocytes and 1 per cent metamyelocytes. Five nucleated red blood cells were noted in a count of 100 white cells. The red cells showed moderate anisocytosis, marked polychromatophilia, moderate macrocytosis and minimal spherocytosis. The initial immunohematologic studies revealed the patient's blood type to be A, Rh_o negative; the direct Coombs test was ++++. The patient's cells washed six times were spontaneously agglutinated when suspended in 20 per cent bovine albumin solution. The patient's serum agglutinated normal com-

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patible cells at 37°, 22° and 3° C., indicating the presence of circulating agglutinins. It was impossible to cross-match the patient with prospective donors with any degree of certainty.

Bone-marrow aspiration showed an intense normoblastic hyperplasia.

The history of increasing pallor and icterus, together with the slight splenomegaly, suggested hemolytic anemia. The peripheral-blood findings of slight spherocytosis, polychromatophilia and marked reticulocytosis further strengthened this impression. The direct Coombs test and the repeated agglutination of prospective donor cells by the patient's serum indicated that this was a case of autoimmune hemolytic anemia possibly symptomatic of an underlying disease, such as disseminated lupus or rheumatoid arthritis. Because of the severe anemia, a transfusion of 500 cc. of washed red cells (Type A, Rh_0 negative) was given soon after admission, with no untoward reaction. ACTH (Wilson)* was also started in a dosage of 20 mg. subcutaneously every 6 hours. On the day after admission the patient received 1000 cc. of washed cells (Type O, Rh_0 negative) for red-cell survival studies. By this time, she was afebrile and appeared greatly improved.

Urinary findings were normal, with the exception of an elevated urinary urobilinogen level. Blood chemical constituents were as follows: total protein, 6.8 gm. per 100 cc., with an albumin of 4.0 gm. and a globulin of 2.8 gm.; total cholesterol 178 mg. (with 64 per cent esters) and total bilirubin of 1.8 mg. per 100 cc. (1.4 mg. indirect reacting); cephalin flocculation of ++++; thymol turbidity of 4.8; and erythrocyte sedimentation rate (Westergren method) 147 mm. per hour. Studies on the stools were negative for occult blood and showed a urobilinogen output of 533 mg. per day (about 15 times the normal value, when related to the hemoglobin value).

Serologic studies revealed many peculiarities:

Both the blood Kahn and blood Hinton tests were positive.

Heterophil-antibody reaction was positive to a dilution 1:56.

Agglutinin against normally compatible cells was present at 37°C. in bovine albumin to a dilution of 1:4, not demonstrable in saline solution. At 22°C. the titer in bovine albumin was 1:16, with questionable activity in saline solution. At 3°C., a cold agglutinin was detected that was active in saline solution to a titer of 1:16, and in albumin to 1:128. Tests using trypsinized erythrocytes with saline dilutions of the patient's serum paralleled the tests in albumin closely. Initially, the only tests performed for hemolysins, using a modification of the acidification technic of Gardner, were negative. Subsequent tests performed by the method of Dacie and de Gruchy on the admission serum preserved at −30°C. revealed an active hemolysin in a titer of 1:32.

Anti D incomplete agglutinin was present to a titer of 1:32.†

Repeated tests for the L. E. (lupus-erythematosus) phenomenon were negative.

The patient displayed a dramatic response to ACTH therapy. After a brisk reticulocytosis to a peak level of 40 per cent on the 9th day of therapy the red-cell count rose to 3,300,000, with a hemoglobin of 11.7 gm. per 100 cc. After 2 weeks of therapy the sedimentation rate was 6 mm. per hour, and the serum bilirubin 0.6 mg. per 100 cc. The autoagglutination had virtually disappeared from the serum and was now detected only in undiluted strength. The direct Coombs test was only weakly positive. The previously positive blood Kahn and Hinton tests were completely negative. (The effect of therapy on the hemolysin discovered later could not be determined during this initial remission because many of the preserved specimens had developed anticomplementary properties.) The patient was asymptomatic, and was discharged on May 9 with maintenance therapy of 100 mg. of cortisone taken orally. On May 10, the red-cell count was 4,180,000, with a hemoglobin of 12.5 gm. per 100 cc. The reticulocytes were 1 per cent, and the serum bilirubin was 0.3 mg. per 100 cc. On May 17 the cortisone dosage was reduced to 50 mg. a day.

On May 22 the patient was readmitted to the hospital with a maximum temperature of 101°F. and pain and swelling of the left leg of 3 days' duration. Physical examination was negative except for swelling of the left leg, edema of the left ankle and exquisite calf tenderness. There was no icterus or splenomegaly. A diagnosis of thrombophlebitis was made, and she was treated with bed rest and Tromexan with an uncomplicated course. During her hospital stay cortisone was also continued in a dosage of 50 mg. a day. There was no evidence of increased hemolysis during this period, as judged by hematologic values, serum bilirubin or fecal urobilinogen output. The direct Coombs test, however, was still weakly positive.

After discharge on June 1 the patient was treated with Tromexan and cortisone on an ambulatory basis. On June 19 Tromexan was discontinued, and on June 28 cortisone was discontinued. Throughout July she did well. Although there was a slight drop in the red-cell count, there was no reticulocytosis or evidence of increasing hemolysis. During the first 2 weeks in August, she noted lack of energy as well as a return of joint pain. On August 13 physical examination showed pallor, with no clinically detectable icterus. Splenomegaly was not present. There was slight swelling of the proximal interphalangeal joints.

Examination of the blood revealed a red-cell count of 2,200,000, with a hemoglobin of 7.4 gm. per 100 cc. and 10.4 per cent reticulocytes, and a white-cell count of 6400, with 71 per cent neutrophils, 26 per cent lymphocytes and 3 per cent monocytes. There was rare spherocytosis and moderate polychromatophilic macrocytosis. The serum bilirubin was 1.1 mg. per 100 cc. (0.7 mg. indirect reacting). The Coombs test was again strongly positive. A circulating serum hemagglutinin active against normally compatible cells was demonstrable at 37°C. to a dilution of 1:2 by both the albumin and the trypsin technic; at 22° the titer was 1:8 with no activity in saline solution; at 3° activity could be found in saline solution to a dilution of 1:2, whereas in albumin the titer was 1:32. Acidification of the serum did not enhance the agglutination, nor did it activate a hemolysin. By use of the trypsin technic of Dacie and de Gruchy, a hemolysin was demonstrated to a dilution of 1:32. The L. E. test was again negative.

It was evident that the patient was in a moderately severe relapse. Cortisone was instituted in a dosage of 100 mg. daily by mouth. There was an immediate, favorable response, the reticulocytes rising to a height of 25.8 per cent in a week. The red-cell count and hemoglobin rose to remission levels in 1 month. In 1 week the Coombs test became slightly weaker, as did the activity of the agglutinin at 37°C. The hemolysin appeared unchanged. By the end of 2 weeks the hemolysin gave signs of decreasing. In 3 weeks the Coombs test was much weaker, and the agglutinin had virtually disappeared. Slight hemolysin activity was still present. By September 25 the Coombs test was weakly positive, no agglutinin activity was present at 37° and 22°, and the hemolysin had disappeared. The red-cell count was 3,980,000, the hemoglobin 11.3 gm. per 100 cc., and the reticulocytes 1.1 per cent. Cortisone dosage was slowly reduced soon after the remission was well established. After slight difficulty, the minimum maintained dosage of cortisone necessary to continue the remission was found to be 50 mg. daily alternating with 25 mg. This therapy has been maintained steadily for 1 year with no ill effects.

At the time of the writing of this report,‡ the red-cell count was 4,100,000, the hemoglobin 13.2 gm., the reticulocytes 1.2 per cent, the platelets 546,000, and the white-cell count 9000, with a normal differential. Serologic studies revealed a negative blood Hinton test, negative heterophil-antibody reaction (1:7 titer), and agglutinin activity in albumin at 37°C. absent against compatible cells, as were tests using trypsinized erythrocytes. At 3°C. the patient's serum agglutinated normal cells suspended in saline solution to a titer of 2, and trypsinized cells to a titer of 32. The Coombs test was ++++. Anti Rh_0 titer was 2.

The effect of the therapy is shown in Figure 1.

*This had the potency of 2 international units per milligram.

†The patient's husband was Type O, Rh_0 positive, and her only son was Type A, Rh_0 positive. There was no evidence of erythroblastosis fetalis at his birth. In addition, it was determined later that on admission to the first hospital, she had been considered to be Rh_0 positive, undoubtedly because of clumping of her "coated" cells with the anti-Rh_0 testing serum. Because of this she had been given 2 transfusions of Rh_0-positive blood. Sensitization probably occurred at this time in view of the failure of any hemolytic reaction during these transfusions.

‡November 30, 1952.

Discussion

The immunologic mechanism in many cases of acquired hemolytic anemia is now widely recognized. Recently Young and his group[15] used the term "autoimmune hemolytic disease" to delineate cases in which an abnormal immunologic mechanism, presumably an autoantibody, can be demonstrated.

The development of an autoantibody has long been considered a violation of immunologic principles. Ehrlich's expression "horror autotoxicus" has dominated thought for many years — so much so that many immunologists even now cannot accept the possibility of autoimmunization. Nevertheless, it is now recognized that autoantibodies may be formed against homologous tissue under experimental conditions. Such antigenic factors as the original locus of the provoking stimulus,[19] the use of nonspecific adjuvants[20] and the route of administration[21] may play an important role in deciding the success or failure of such experimental attempts. In clinical practice it must be confessed that little is known concerning possible antigenic factors or, indeed, whether antigens in the true sense are involved. Of far greater importance seems to be an inherent characteristic of the individual — namely, the ability to respond to certain stimuli by an outpouring of antibodies. That individual differences in antibody production exist has been long recognized. It is also becoming apparent that the enhanced capacity of certain persons to form antibodies is not always a desirable feature and may even be responsible for certain types of illnesses,[22] which might be classified as "immunoallergic." Such diseases are autoimmune hemolytic anemia, rheumatic fever, glomerulonephritis, idiopathic periarteritis nodosa and disseminated lupus erythematosus.

Regarding the last disease mentioned above, evidence is accumulating rapidly that some type of hyperimmune process is an important pathogenetic mechanism.[23] The isolation by Haserick[24] of a serum L. E. factor responsible for the Hargraves phenomenon and present in the gamma-globulin fraction is indicative of this view,[25] especially since it disappears during remission.[26] Aberrations of the immunologic mechanism extend in this disease not only to the production of opsonin-like globulin but also to other bizarre autoantibodies. There are numerous reports of autoimmune hemolytic anemia associated with lupus erythematosus[23, 27-29] in which antibodies against the patients' own cells were demonstrated.

The ability of such persons to form antibodies while assuming its most bizarre manifestation when autoantibodies are produced extends also to the production of isoantibodies and even heteroantibodies. Callender and Race[30] have reported a remarkable case of lupus erythematosus in a patient who received numerous transfusions. There was evidence of multiple iso-sensitization to 5 blood groups, 3 of which had never previously been discovered. Wiener[22] has noted the ease with which persons suffering from autoimmune hemolytic anemia become sensitized to blood groups of usually low antigenicity. Finally, mention should be made of the frequent occurrence of so-called "biologically false-positive" tests for syphilis encountered in lupus erythematosus, periarteritis nodosa,[31] autoimmune hemolytic anemia (L. Sanchez-Medal[32]) and so forth. This, too, seems to be a manifestation of a heightened capacity to form antibodies, in this case against lipid antigens. Kahn[33] stated: "False positive reactors apparently have developed a

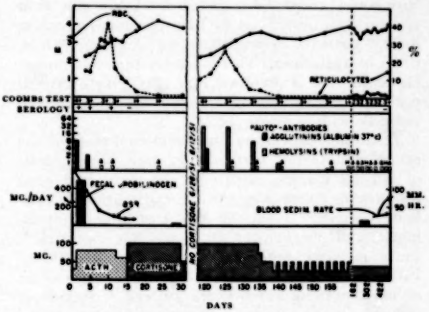

Figure 1. *Results of Cortisone and ACTH Therapy in a Patient with Autoimmune Hemolytic Anemia.*

capacity to give intensified universal reaction . . . this intensified precipitation manifests itself in the central zone of the universal reaction which embodies the serological reaction for syphilis."

The case reported above is an excellent example of the enhanced ability of some persons to produce varied types of antibodies. Thus, it was possible initially to demonstrate a red-cell coating antibody, a nonspecific red-cell incomplete agglutinin, a red-cell hemolysin, anti-RH_0 incomplete agglutinin, and heterophil antibody. Although repeated tests for the Hargraves phenomenon were negative, the clinical symptomatology of the patient was strongly suggestive of disseminated lupus erythematosus.

It was difficult to decide which of the antibodies present was the causative factor of the hemolytic state. It seemed fairly certain that the coating antibody, which could only be demonstrated by the antiglobulin method, was not per se an important factor. In vitro this antibody caused neither hemolysis nor agglutination, and we have now encountered many treated cases of autoimmune hemolytic anemia in which coated cells were present,

but evidence of hemolysis was lacking in vivo. On the other hand, it cannot be denied that at times the Coombs procedure is the only immunologic test that is positive in the presence of frank hemolysis. A mechanism whereby coated cells are more liable to phagocytosis by the spleen and other organs of the reticuloendothelial system could explain this discrepancy in vitro. In the case reported above, the Coombs test remained positive, although there was no evidence of increased hemolysis. However, since tests of red-cell survival time were not performed during remission, a slight decrease in red-cell span may have been present in the absence of the other features of increased hemolysis.

Evaluation of the role of incomplete agglutinin is open to similar difficulties. Agglutination in itself does not cause hemolysis. Some degree of inverse correlation exists between serum agglutinin titer and survival time,[34] but we have observed, as others have,[12] patients in remission with extremely high titers of agglutinin. This indicates that some other factor in vivo is involved that may play a critical position in determining whether the agglutinated red cells will be destroyed.

This may depend on the functional state of the reticuloendothelial system regarding phagocytosis of red-cell masses, explaining the occasional good response to splenectomy without alteration in antibody pattern,[35] or on the extent of increase in osmotic and mechanical fragility that agglutinins cause in vivo, rendering the cells vulnerable to varied trauma[36]; or it may depend on the release of substances injurious to the red cell derived from ischemic tissue whose blood supply has been compromised by agglutinative thrombi.[37] Finally, in the clinical state, eventual destruction of red cells may not always depend on the action of agglutinins but rather on the presence of accompanying hemolysins. As pointed out above, the failure to detect such immune bodies may be more technical than real.[15]

When both agglutinins and hemolysins are detected in the same case, it is possible that multiple hemolytic mechanisms are involved. Hemolysins in the presence of complement can destroy red cells without the aid of any other agency. Observations in the case presented above indicated that both the agglutinin and hemolysin disappeared at a point where there was a cessation of increased hemolysis, therefore shedding no light on the relative importance of one or the other. Objections might be raised about the significance in vivo of a hemolytic mechanism that in vitro requires a gross alteration in red cells — namely, trypsinization. Similar objections might be raised concerning other conditions required to demonstrate hemolysin in vitro such as acidifying the serum to pH 6.5. Yet, as Dacie[12] has pointed out, " . . . it is difficult to believe that the ability of the antibodies to cause hemolysis in vitro is entirely without significance." No one would even remotely concede that the pH of the blood in vivo approaches 6.5, even nocturnally, but such a pH range must be achieved in vitro before the hemolytic mechanism of paroxysmal nocturnal hemoglobinuria is demonstrated. Ponder[38] has stated that a great gap exists between knowledge of hemolysis in vitro and that in vivo. Present indications seem to signify that exaggerated conditions are sometimes necessary for test-tube demonstrations of hemolysis that in the body seem to be activated by only slight departures from the norm.

Under the influence of ACTH and cortisone, a definite reduction and eventual disappearance of the hemolysin, incomplete agglutinin and antibody against lipid antigens was effected. Reductions in the titer of anti-Rh_0 antibodies and heterophil antibodies were also noted, but were well within the levels of spontaneous decline observed in untreated cases. A complete discussion of the effect of these hormones on antibody production is beyond the scope of this paper. Nevertheless, we have noted consistently the ability of such agents to suppress autoantibody formation in autoimmune hemolytic anemia and in doing so to control the rate of hemolysis.[38] More precise immunologic studies in animals by Germuth, Oyama and Ottinger,[39] Bjørneboe et al.[40] and De Vries[41] indicate that such an effect on the antibody-producing tissue does occur. Present evidence does not confirm earlier contentions that such hormones affect antigen-antibody reactions by catabolism of already formed antibody[42] or by otherwise interfering with these reactions.[43] The ability of these hormones to cause regressive changes in the lymphoid apparatus simultaneously with antibody decline[12, 40] suggests that they are effective in autoimmune hemolytic anemia at this fundamental tissue level.

Summary

An unusual case of autoimmune hemolytic anemia is described in which multiple, varied antibodies were present. A nonspecific "coating" antibody, incomplete agglutinin and hemolysin were isolated as well as lipid antigen antibodies (Kahn), heterophil antibody and incomplete anti D. ACTH and cortisone effected remarkable control over the hemolytic process, with total suppression of the agglutinin and hemolysin but only partial eradication of the coating antibodies. The factors contributing to autosensitization and the relative importance of the various antibodies in causing the clinical picture are discussed.

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CONTRIBUTION OF S. RAMON Y CAJAL TO THE KNOWLEDGE OF THE ANATOMY OF THE CEREBRAL CORTEX*

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A CENTURY after the birthday of Cajal,[1] it is fitting to recall his words when he received an honorary degree from Clark University in 1899:

> This honorary distinction, as well as the invitation which Clark University condescended to make me to take part in the conferences for solemnizing the tenth anniversary of its foundation, shows once more that men of science know no frontiers, and that they form a universal family, whose solidarity and fellow-feeling place them high above the wrangle of material interests and selfish struggles of nationalities. . . . I trust that the creation of Clark University may give the signal for founding in America other similar institutions embracing a still larger number of branches of science, and having as their primary object the wresting of secrets from nature, supplying industry and arts with principles and facts capable of fruitful applications, forming the research spirit of the new generation, freeing it from the clogs of routine and imitation, and finally forming the foundation of a splendid civilization superior in groundwork, as well as in form, to that of the European nations.

Cajal's contributions to the knowledge of the structure of the nervous system came principally from his use of the silver-staining technic of Golgi,[2] but he also employed the methylene blue method developed by Ehrlich.[3] He made modifications of the silver procedure that are now designated by his name. He improved the technic and greatly extended the work of Golgi.

The earliest available paper by Cajal[4] that is related to the cerebral cortex appeared in 1890.

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It gives the results of an investigation of the connections of the elements of the retina in birds.

His next paper, which appeared in 1891,[5] was an extensive and intensive study of the cerebral cortex of the rat, mouse, rabbit and guinea pig. He described the cells and fibers in the various layers of the cortex. In this paper he illustrated some new structures, which he called "spines," on the dendrites of the pyramidal cells. This was the first record of the observation of these structures. He did not say much about them in this paper, and located them only on the terminal branches of the apical dendrites. During the following year several investigators in various countries presented papers verifying the presence of these structures on the dendrites of nerve cells.

In 1894 a book by Cajal[6] was published in Paris. Two chapters devoted to the cerebral cortex described the cells in the various layers of the cortex and discussed the distribution of their axons. The fibers in the cortex and in the white substance, including projection and association fibers and those of the corpus callosum, were also described. The cells and fiber connections in the cornu ammonis and fascia dentata were considered in detail. On the basis of the study of the cerebral cortex in lower vertebrates Cajal offered his ideas on the evolution of the nerve cells. In this book he also described the cells, fibers and fiber connections of the olfactory bulbs and of the retina. A second edition of the book was printed in 1895.

In 1899 Cajal[1] delivered three lectures at the decennial celebration of Clark University. He spoke in French, but the lectures were published in English in the volume commemorating that occasion. In this he described the visual and sensorimotor cortex only of man and higher mammals, and included a few observations on the structure of other sensory regions:

> There are two camps of neurologists, the unicists and the pluralists. The unicist doctrine proclaimed by Meynert and reaffirmed quite recently by Golgi and Kolliker, supposes that all regions of the cortex possess essentially the same structure, functional diversity being due to diversity of origin of afferent or sensory nerves. This amounts to saying that cerebral specific energy of nerves is the necessary effect of the particular organization of each sense as well as of the special character of the stimuli received by the peripheral sensory surfaces, skin, retina, organ of Corti, etc.
>
> The pluralist doctrine, upheld recently by Flechsig, without rejecting the particular influence of connections with different nerves, maintains that diversities of function result also from particular structure of each cortical area.

Cajal favored the pluralist doctrine, asserting that his "researches tend to prove that the topographical specialization of the brain depends not only on the quality of the stimuli analyzed and gathered up by the sensory mechanisms, but also on structural adaptations which the corresponding cerebral areas undergo." He added, however:

> We must not carry to an extreme the structural plurality of the brain. In fact, our researches show that while there are very remarkable differences of organization in certain cortical areas, these points of difference do not go so far as to make impossible the reduction of the cortical structure to a general plan. In reality, every convolution consists of two structural factors: one, which we may call a factor of a general order, since it is found over the whole cortex, is represented by the molecular layer and that of the small and large pyramids; the other, which we may call the special factor, particularly characteristic of the sensory areas, is represented by fibre plexuses formed by afferent nerve fibers and by the presence at the level of the so-called granular layer of certain cell types of peculiar form.

Many descriptions of the visual cortex had appeared before Cajal's work, but they had been limited to methods that did not stain the axons and dendrites of the nerve cells. In this work Cajal recognized nine layers in the visual cortex, and he described the cells and fibers in each layer, giving the distribution of all the fibers.

Papers and books crowded upon one another in rapid succession during the next few years. In 1899 appeared the first of two volumes written in Spanish on the structure of the nervous system of man and the vertebrates. The second volume, consisting of two books each containing 600 pages, was printed in 1904,[7] the cerebral cortex being described in almost 400 pages of results of observations and beautiful illustrations; one chapter was devoted entirely to theoretical considerations of structure and function.

From 1900 to 1906 he wrote five volumes covering studies on the cerebral cortex of man; these were translated from Spanish into German by Bresler.[8] Each of the following areas of the cortex was described in a volume: the visual, sensory motor, acoustic and olfactory. The last volume was devoted to a discussion of comparative structure of cells in the cortex, the histogenesis of the cortex and anatomicophysiologic considerations.

In 1909 appeared the first of two large volumes on the histology of the nervous system written in French.[9] The second volume, which was printed in 1911, described the structure of the cerebral cortex in man and vertebrates, the histogenesis of the cerebral cortex and anatomic and physiologic considerations. The discussion of the cerebral cortex was almost an exact duplication of the discussion in the second volume of a previous work.[7] The same order of presentation of material and the same plates were used in both books. The first volume, considering the histology in French,[9] described the "spines," which he had discovered in 1891 on the dendrites of the pyramidal cells. These structures were demonstrated by both the Golgi and Ehrlich methods. Cajal had no knowledge of the function of these structures, but speculated regarding them: "Do they absorb perineural lymph for the nourishment of the dendrite?" Were they, as Berkeley had suggested, the apparatus of charge, the collectors of nerve current, comparable to the points of a static electricity machine or the brush of a dynamo? "We ourselves place our preference to this latter

opinion, as being more probable, all the more as this agrees with our own ideas." Cajal suggested that these structures greatly increase the receptive surface of the dendrites, and that they bring the contacts between terminal axon arborizations and the dendrites closer together.

The Spanish edition of Cajal's extensive investigation of degeneration and regeneration of the nervous system, published in 1913, consisted of two volumes of about 400 pages each. An edition of this work in English was published in 1928.[10] The degenerative and regenerative process in the cerebral cortex was discussed in the second volume. The experimental work was performed on young mammals, such as the cat, dog and rabbit. This truly enormous work scarcely falls within the scope of this paper, but it should be consulted in a study of the subject.

One of Cajal's most important contributions was to prove beyond doubt that every nerve cell is individual, and not part of a syncytium. He credited W. His (1886) and A. Forel (1887) with first advancing this idea, but through his extensive investigations by the use of the silver method, which stains dendrites and axons as well as cell bodies, he produced convincing evidence that this conception of the nervous system is correct. His last paper,[11] published posthumously in 1935, is a splendid treatise defending this concept. In a masterful manner Cajal marshaled evidence from all parts of the nervous system, including the cerebral cortex of man and lower vertebrates, and from all phases of his extensive investigations to demonstrate the individuality of the neuron on the basis of anatomy, embryology, phylogeny, physiology, regeneration and pathology.

I have done little more than list the works of Cajal in which the cerebral cortex is discussed; this is all that can be done in the brief time allotted for this paper. His enormous contribution to knowledge, his careful objective observations, the beautiful presentation of results, and his modest attitude fill one with respect, admiration and gratitude.

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MEDICAL PROGRESS

HEALTH IN COLLEGES

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IT has been nearly a century since a college president publicly stated and recorded his concern over the special problems centering around health in colleges. President William A. Stearns, of Amherst College, in 1856, declared that, "The breaking down of the health of the students, especially in the spring of the year, which is exceedingly common, involves the necessity of leaving college in many instances, and crippling the energies and destroying the prospects of not a few who remain, is in my opinion wholly unnecessary if proper measures could be taken to prevent it."[1] What those proper measures are and how they can be brought to bear on the student has not yet been fully determined. In 1861 Amherst itself established a comprehensive program, consisting of medical examinations, physical exercise and clinical care. The new "Department of Hygiene and Physical Education," the first of its kind in America, was headed and developed for the next half century by Professor Edward Hitchcock, a physician who had graduated from Harvard Medical School in 1853. For twelve years, from 1898 to 1910, he was also dean of the Faculty.[2] For many years this program stood alone, but in the last few decades almost every college has made at least some effort to meet the health needs of its students.

The health of college students, when left entirely to the community medical resources, leaves much to be desired. Students underestimate the possibilities of illness or injury, they are usually under heavy financial pressure, and they are willing to take risks. Accordingly, they tend to proceed on the assumption that health is a matter that will take care of itself. They may neglect to get a bal-

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anced diet, and they may stay in their rooms when ill, not knowing whether they are wise in doing so or whether they are endangering others. When prolonged and expensive illness strikes, they may have to leave school permanently unless their families are financially able to rescue them. For these and similar reasons, it has become increasingly apparent to most college authorities that the health of college students is of concern to them, that it cannot be left entirely with the individual and the community, and that special measures are justified in meeting the problem.

Before the provision of on-campus medical facilities, the usual custom was to engage the services of a local physician to come to the college for regular office hours, largely for purposes of diagnosing, advising and referring the sicker students to medical or surgical consultants or hospitals in the community. This soon led to the allocation of special quarters, much in the nature of a dormitory adjunct, for students who had to be in bed a few days but who were not seriously ill. Additions to this type of service led gradually to the establishment of college infirmaries, some of which are large and elaborate and possess facilities and equipment identical with those of a community general hospital.

As soon as the extensive variety of student health problems became recognized because they were all brought to the attention of one person, a number of questions arose. What are the causes of ill health? What preventive measures can be taken? Are the periodic outbreaks of gastrointestinal disorders inevitable? Who advises the students on health matters? How can the heavy expenses of the few students with severe illnesses be met? And what about the emotional disturbances noted alike by physicians, faculty members and people in the community?

To answer these and many related questions a new focus of interest — student medicine — has appeared in the last few decades. It is not like the specialties in which a certain part or system of the body is selected for extensive consideration. Rather, it is a special point of view toward young persons in the process of attaining an education. It calls for physicians who think in terms of prevention as much as treatment and of the reaction of young men and women to a new physical, intellectual and social environment in both health and disease. A larger role is required of the college physician than his time-honored and vital function of restoring the sick and injured to their former effectiveness, so far as possible. His job is to devise ways and means of demonstrating how medicine can contribute to the development and efficiency, not to say happiness, of all the members of the college community.

The practitioner of medicine has the entire human being to consider, and in addition he must think in terms of all his many relations with others. So far as the comfort, well-being and happiness of the patient are concerned the advances made by medicine since the successful demonstration of anesthesia in 1846 are the most important to him of any area of knowledge. Not only is health desirable for happiness but also happiness is essential for health. Medicine constitutes a peculiarly advantageous platform from which to view man in all his complexity. Though regarded as one of the sciences, it is also one of the humanities and has much to offer to the education of every citizen. Its contributions must be indirect and perhaps general, but they are no less needed because of that.

Progress in this field has quite naturally been uneven. Some colleges are small, their financial resources are sharply limited, they are situated far from urban medical centers, and they cannot possibly develop ideal medical services. On the other hand, their smallness and relative isolation may favor a type of desirable health service and education that could not readily be provided in the large, busy university. Each institution must work out its own program in the light of its own resources and needs, guided by the general principles of hygiene of the college age group. It is largely with such principles that this review is concerned.

Clinical and Epidemiologic Considerations

The clinical problems presented by college students do not differ in any essential way from those of any similar age group. Respiratory infections and trauma are the two largest single classes of problems encountered. Infectious mononucleosis, pneumonia, infectious hepatitis and gastrointestinal disorders constitute the more common syndromes in internal medicine. Mental and emotional disorders take up a large portion of the physician's time. This confirms the idea, mentioned above, that a college physician should be interested primarily in the applications of medical and hygienic principles to a comparatively healthy population rather than in the treatment of disease alone.

A fully equipped health service that has been well accepted by the college community can easily expect about 5 to 8 clinical visits yearly from each student. The use of college infirmaries has numerous variations not easy to explain. The average infirmary census in a residential college is apt to be proportionally higher than that in one with a large commuter population, mainly because mild illnesses are treated at home. In recent years there has been a tendency in many colleges for the number of patient days to decrease. Typical of this decrease is the experience at the Massachusetts Institute of Technology, where the number of patient days was 3512 in 1946–47 and 3792 in 1947–48, whereas it was 2827 in 1950–51 and 2948 in 1951–52. Whether this is due to better clinical and outpatient care, improved general health measures in the community,

increased use of antibiotics or other circumstances is not known.

Communicable diseases do not form nearly as great a hazard to the college student as to the preparatory-school student, presumably because by this time most of the students have had the common types of contagious diseases. An exception is infectious mononucleosis, which is particularly common in student infirmaries, a notable example being at Harvard University during the period 1935–43, when 196 cases were reported by Contratto.[3]

Most colleges insist on a smallpox vaccination within three years as a prerequisite to admission. Tetanus toxoid is occasionally required, as at Massachusetts Institute of Technology, where the problem of serum sickness after tetanus antitoxin has virtually disappeared.

Most colleges do not extend medical service to faculty members and employees on an extensive scale. First-aid and emergency treatment are nearly always given, and the administration of pension plans and industrial-compensation regulations necessitate considerable medical contact. Care of faculty and employees presents many difficult problems, particularly those involving methods of payment for such services and relations with physicians in the community.

Administrative Relations

The relation of the health services to the administration of the college or university is frequently of great importance. The director of the health service reports to the dean of students in some institutions and to the provost or an official of similar rank in others, but in most he reports directly to the president — an arrangement that is strongly favored by directors of health services for many reasons. Services that report directly to the president are in general the strongest and most progressive. If health issues are important, they should be known at the highest level. Many aspects of the information that the college physician possesses must be used with the greatest consideration for the welfare of the patient, and in such cases it is often of great advantage for the president to be made aware of delicate situations directly by the physician. This is no less true in large universities than in small colleges, though, of course, in the former, the president would be informed of only the major issues that might arise, his assistants relieving him of the responsibility of routine matters. Finally, the health service itself, and the individuals who comprise it, will be enabled to work most effectively if it is well known that the president is really interested in health, aware of the many problems in this field and desirous of increasing, enlarging and expanding the contribution of medicine, particularly preventive medicine, to the process of developing intellectually and emotionally mature students.

Surveys of Health Facilities

The planning committee of the Third National Conference on Health in Colleges made a survey of current college health practices in 1945–46. Information was sought from more than 1000 colleges, but the final summary was based on 300 colleges that submitted reasonably complete reports, based on a student population of more than 1,000,000.

The committee noted that most college health programs had expanded in both extent and scope since previous studies had been made. It further pointed out[4]:

> The tendency seems to be in the direction of centering direct administrative responsibility for all parts of the health program, except physical education, in the health service or in the person of its director or college physician. Formerly, many of these activities were carried by a department of hygiene and/or physical education or department of biology. Even classroom instruction in health appears to be shifting toward a medical approach. Interest in environmental sanitation is increasing and responsibility for it seems to be shifting from administrative officers to health services or to an official public health agency.

Two thirds of the colleges had special student health fees. For all types of colleges the number of full-time physicians was slightly more than 1 per 1000 students, and the number of nurses slightly more than 2 per 1000. About half the colleges had some "medical counseling in mental hygiene." One out of 8 extended medical care to the faculty.

Dickinson and Welker,[5] of the American Medical Association, in a study of university and college health facilities in 1949–50, collected much information but found considerable difficulty in interpreting it. A twelve-page questionnaire was sent to 1124 universities and colleges, and satisfactory replies were received from 462. The authors concluded that great variation existed in the facilities, personnel and services available to students. Some check on the health of new students is made by almost all colleges with health services; 70 per cent required a routine health examination, and 25 per cent accepted a family physician's report instead. Medical treatment for ambulatory student patients involving more than "emergency care only" was reported by 88 per cent of the colleges. This service was most commonly provided by the health service staff and only rarely by outside physicians. Bed care for students was provided in a college infirmary by 62 per cent of the colleges, in a college hospital by 11 per cent, and in a community hospital by 32 per cent. In only 10 per cent was major nonemergency surgery done. Ophthalmologic and dental services were not usually provided to the students by the college health services. In general, the larger the college the more inclusive the health services. Student health services were usually financed by a special fee (48 per cent) or by a fee included in tuition (29 per cent). Outside insurance was optional in 11 per cent and required in 4 per cent of the colleges. The data on the care of faculty

and other employees was not satisfactory, but only a few colleges provided health services for them. In the survey material it was impossible to get any adequate idea of the cost of such health services. Mental health services were rendered to students by a health-service physician in 31 per cent of the colleges, by psychologists in 22 per cent and by a student personnel officer in 19 per cent.

Athletics

Co-operation is required in the relation between athletic departments and health services in any college. It is generally agreed that coaching and medical supervision should work hand in hand. At the Third National Conference on Health in Colleges[6] all the physicians, physical-education personnel, coaches and athletic directors present officially agreed that any athletic program should be administered and financed by the college just as any other department. Opportunities should be available for all students to participate if they wish to do so. Medical examinations should be given at the beginning of each season and as frequently as needed during the season. Medical service should be available at all regularly scheduled contests. A physician should always decide when an injured student is to return to full activity and should supervise his treatment while he is out. Every reasonable precaution should be made to prevent injuries. All these principles are basic, but under the pressure of the various forces aiming at successful teams, observance is not always easy.

Reid and Swan[7] analyzed the football injuries at Northwestern University during 1950–51. There were 120 injuries among 70 players engaged in 255 practice sessions and games accounting for 15,750 player days. The most frequent (34) as well as the most serious injury was one involving the knee joint. The other types of injuries in order of frequency involved the ankle (19), shoulder (12) and rib cage (12); lacerations numbered 11. There were only 4 head injuries. The authors noted that the bulk of injuries occurred in the early days of the spring practice and in the fall before the first game. Most injuries occur when the players get tired or relaxed.

In a review of athletic injuries, Thorndike[8] recently emphasized the need for competent supervision of injuries. He pointed out that trauma of all types constituted 20 per cent of the diagnoses of students at Harvard during the ten-year period, 1942 to 1952. Of these, 15 per cent were quite serious — that is, were made up of fractures, dislocations or visceral trauma. He emphasized the fact that ligamentous injuries may be quite as serious as those with fractures or somewhat more obvious signs of trauma. He has not found it necessary to prohibit sports competition after injury but has always been able to find some suitable athletic activity in which the student could profitably engage. He points out that many students can participate in crew, track, swimming, squash or tennis instead of contact sports and still have the feeling of being in strenuous competition.

He states specifically that no student should return to body-contact sports who has had a fracture-dislocation, a large laparotomy or nephrotomy scar, removal of spleen or kidney, three cerebral concussions of moderate degree or one with brain lacerations, or the loss of an eye.

Tuberculosis Control

The problem of tuberculosis control has long been of primary interest to college health physicians. It is similar in some respects to the problems of mental health. Frequently, both do not have conclusive symptomatology and hence their management requires a special kind of alertness and planning. In addition to the fact that tuberculosis is the chief cause of death in the college age group, there is the worthwhile stimulus to the educator of demonstrating to the student the advisability and technics of stamping out a disease. According to Durfee,[9] "The ideal plan for tuberculosis control for a college calls for a tuberculin testing of all new students with annual retesting of non-reactors; for the chest x-ray of all new students regardless of their reaction to tuberculin, and for the annual chest x-ray of all tuberculin reactors." Durfee[10] had earlier reported that in 149 colleges with no tuberculosis control program, 9 cases of active tuberculosis were discovered in 101,518 students. In 312 colleges that did have some definite control program, 389 cases were found among 357,714 students. Thus, twelve times as many cases were found in colleges where a program was in effect, as in those with no special program.

Unfortunately, it is difficult for many colleges to carry out the ideal program of tuberculosis control. Sometimes this is due to lack of funds, but in the larger universities, the task of administering this program to a large group of students widely scattered in their various living quarters and under heavy demands from the curriculum and extracurricular activities is practically insuperable. In many of the larger schools a compromise has been reached by having a chest x-ray examination on each entering student with a repeat film at yearly intervals. No test is a substitute for clinical awareness of the possibility of tuberculosis in those with low-grade symptoms.

Christie[11] recently reported that the mortality from tuberculosis in the United States decreased from 40.1 per 100,000 in 1945 to 22.2 per 100,000 in 1950. He stated that there are now definite signs that the battle against the disease is reaching its final stages. It is too soon for such optimism, however, in the colleges.

Occupational Medicine

In the largest universities, particularly in the last fifteen years, certain research programs have developed that present unusual health hazards such as the use of physical equipment involving previously unknown levels of radiant energy. In addition various operations entailing exposure to mercury, carbon tetrachloride, benzine, beryllium, germanium and similar materials are potentially dangerous. At the Massachusetts Institute of Technology this problem has been met by the establishment of an occupational medical service within the Medical Department.[12] Its staff consists of a chief, who is also assistant medical director, and an internist and industrial toxicologist, another physician of similar training and experience, a physician who is also a biophysicist, a radiologic safety officer and an engineer trained in public-health problems, a chemist, electronics technicians and monitors. This staff is constantly engaged in field trips to operations of potential hazard or in planning safety programs at laboratories where mishaps have occurred. It also engages in teaching and research activities and serves on a special safety committee made up of about 40 persons distributed throughout the campus according to special geographic areas.

Research

Research in college health services is pursued with considerable vigor in some of the large centers. Among the studies that are well known are those of Hinckley and Hermann[13] in group psychotherapy, Hudson[14] on the incidence of histoplasmosis, Thorndike[15] on athletic injuries and their prevention, and the Grant Study at Harvard.[16, 17] In general, however, research activities in most college health services are extremely limited.[18] This may be due to indifference, to faulty organization, to lack of funds or facilities or, in occasional cases, to the belief on the part of administrators that research by health services is inappropriate since some student funds might be involved.

If research is regarded as a separate activity involving special teams and large sums of money, there is little opportunity for it in most college health services. If it is thought of as curiosity and an eager attitude of mind carried on by careful checking and recording of clinical observations, there is much opportunity for it in these services. Areas that are in particular need of additional research include methods of furthering health education, particularly in large institutions, practical screening procedures for admission, early recognition of serious diseases, control of respiratory infections, prognosis of students who have severe mental illnesses, development of a usable nomenclature of emotional disorders, problems of minority groups, the college environment in relation to health and student counseling, to name only a few.

Mental Hygiene

Although concern for the health of students was first officially expressed by President Stearns of Amherst College in 1856, it was not until about 1920 that major specific interest began to be shown in the emotional needs and problems of college students. The beginnings at Washburn College, West Point, Dartmouth, Vassar and Yale[19] were tentative and experimental, but were based on a feeling of necessity that something must be done about the large numbers of students who had real troubles that did not fit into the commonly accepted categories of academic or medical problems. Although about 550 psychiatrists now do some consulting for colleges, not more than 25 devote their full time to educational institutions.[20] Thus, many colleges are not meeting the situation adequately even yet, and some of those trying to do so find that the difficulties are complex and frustrating. A committee of college psychiatrists with the aid of consultants from education and related fields has recently analyzed this problem in an attempt to clarify methods for using psychiatric skills most advantageously.[21]

This report suggests that, since demands for individual treatment are always overwhelming whenever a psychiatrist becomes attached to a college, a college psychiatrist work as much as possible through faculty members, the administration and community groups, to the end that obstacles to the attainment of intellectual and emotional maturity be removed or minimized. Thus, he will work on educational matters with his colleagues, serve on committees, consult with disciplinary bodies, aid the counseling programs and foster in every possible way the concept that emotional maturation is a part of intellectual growth and hence a legitimate function of education.

The university with the best all-round psychiatric program for many years that most nearly exemplifies the principles suggested above is Yale. Fry[22] has reported a case load for individual treatment varying from 128 to 706 students yearly, representing roughly 3 to 9 per cent of the total enrollment. Other observers put the need higher than that, but for many reasons there are always students who need help but cannot get it or will not accept it. Fry thinks of Yale's service as, "a team of psychiatrists, psychologists and social workers, dealing with the emotional problems of students in a clinic which has become an integral aspect of everyday life in the University [and in which] research is an indispensably vital part." He points out that in addition to helping the student cope with the immense strains on him, the psychiatrist is in an ideal position to study the causes of success and of failure, the effect of the complicated educational

environment on the student and the relation between the individual and society generally.

In comparison with the case load at Yale, Hinckley and Hermann[23] and their associates at the University of Minnesota saw about 1000 patients each year from 1948 to 1951, the total enrollment varying from 25,084 to 28,312. Each new patient was seen on an average of five and three-tenths hours for that year. That university also has an extensive counseling service not directly connected with the psychiatric service, and its figures are not included in those given above. Hume,[24] of the University of California, reported that in the first year of the mental hygiene clinic, (1946–47) she and her colleagues saw 559 students for an average of five and a half hours each, and in the following year this number climbed to 864 for an average of nine and two-tenths hours per patient, including two and four-tenths hours of psychologic testing or interviewing. The Massachusetts Institute of Technology figures for 1951–52 with 5000 students enrolled included 285 students for an average of eight hours per person, and in addition a psychologist spent half his time in testing and interviews. From many exchanges of experiences with others working in this field, I am convinced that once a psychiatric service is well accepted and established in a college the case load is practically determined by the capacity of the staff to find the time to see those requesting help.

The type of psychiatric illness encountered is not essentially different from that seen daily by the general physician or by the psychiatrist in private practice with two exceptions. The first of these is that the problems of older age groups are not present, at least in students; secondly, the students are for the most part "fresh from their symptoms" and have usually not built up long standing and elaborate defenses. Accordingly, the psychodynamics of the illnesses can usually be delineated much earlier than in hospital or private practice. Psychiatrists coming into this field from other types of clinic or hospital activities frequently comment with surprise on how much can be accomplished in a few interviews. Any existing systems of nomenclature are unsuitable when applied to the problems of the college age group. A résumé of experiences in the applications of psychiatry to higher education has recently been published.[25]

Experience and studies in progress by the psychiatric staff of the Massachusetts Institute of Technology indicate that the main obstacles to the attainment of mental health have had their origins for the most part in childhood. Lack of warm feeling from parents may have caused the patient to feel rejected. Faulty discipline may have hindered the development of a sense of security. Lack of positive masculine traits in the father and positive feminine traits in the mother may have produced difficulties in identification. An apparent lack, from the child's point of view, of emotional flexibility in the parents may have incited undue rebellion. Distorted or squeamish parental attitudes about toilet and sex activities leave residual effects that are frequently difficult to eradicate. Parental friction, with its causal or resultant neurotic behavior, makes warm emotional expression by the child difficult or impossible, since expressing love for one parent may seem to him to be risking the loss of love of the other. And, finally, the neighborhood environment in childhood may have had many unhealthy features. These and similarly harmful influences have combined in various proportions to make the student more vulnerable than he would otherwise have been. Accordingly, when he meets difficult situations that call for straightforward, resolute action, he may not be able to devote all his energies to their resolution but may instead fall back on unsuitable and unsatisfying methods of meeting them. Thus, he escapes into boredom, motion pictures, excessive extracurricular activity or overwork or develops symptoms that serve to becloud the main issues. Projection of difficulties to the poor instructor, the unreasonable schedule, the noise in the dormitory, the attitude of the administration, the appearance of the buildings, or to dozens of things or relations in his life becomes quite logical to him.

The desirable goals that appear to be most relevant to the college group in the attainment of maturity include the development of meaningful communication between student and teacher in all areas, in and out of the classroom, a feeling of belonging, great consideration for the individual in all situations but with no lowering of scholastic standards, and a general attitude of tolerance for the unusual but with strong forces tending toward true self-discipline. As many of the problems as possible should be worked out in the context of the usual intellectual and social relations between teacher and student.

The psychiatric service has for basic goals not only the care of students who are disturbed but also the organization of knowledge of human beings as presented by psychiatry generally and derived from therapeutic experience with students particularly, in such a way as to make this knowledge available and useful to the teacher in his responsibility of aiding the optimum development of the student.

The methods of developing an awareness of psychiatric principles among teachers are not yet well defined. Both the educator and the professional worker in this field are concerned with the well known fact that acquiring knowledge about motivation that has a personal, emotional meaning to the reader does not form a simple learning process. There is a tendency to learn what is imparted in a detached intellectual fashion. Under stress one is then apt to behave as though such information had not been acquired. The unconscious patterns assert themselves even though inappropriate and in

spite of existing conscious knowledge of what in retrospect seems more appropriate behavior. The many aspects of this problem can probably be studied more effectively through the medium of conferences and informal exchanges of information between the faculty member and the psychiatrist. These informal day-by-day crisis-determined contacts between the specialist and the educator constitute the greatest opportunity for dissemination of helpful information or attitudes. By these means all persons connected with a college can be made aware of the need for considering emotional growth at the same time the intellect is developing.

Costs and Methods of Payment

Because of the widely varying practices of different colleges and universities, it is extraordinarily difficult to find out the real cost of student health services. The survey made by the American Medical Association in 1949–50, which was the most complete of its kind so far, failed to elicit this information. Accordingly, the following discussion is based to a large extent on personal experience and exchange of information with many other health services rather than from published reports of surveys.

It is obvious that the smaller the college, the higher the per capita cost for adequate health service. Accordingly, it is not at all unusual for the health service to cost from $40 to $80 or more for each student in schools or colleges that have enrollments less than 1000. In two universities with which I am fairly familiar the cost of maintaining adequate medical service for the academic year of two semesters is approximately $35 per year per student. The chief difficulties in calculations of the true cost of health services involve such matters of bookkeeping as heat, light, maintenance, depreciation, taxes, if any, janitorial service and coverage for athletic events.

A usual custom is for the college to assess a health fee to the student, ranging from $5 to $15 per semester, depending on the type of service furnished and the proximity to medical centers. In some institutions no fee is charged, but general funds of the college are used for partial maintenance of the health service, and this is supplemented by an insurance plan whereby the student may protect himself against unusual medical expenses. Typical of the first plan is Harvard University, which charges a regular health fee, for which ordinary medical and surgical services are rendered together with two weeks in the college infirmary or a hospital connected with the medical school and certain other privileges as well. Typical of the second plan is the Massachusetts Institute of Technology, which appropriates money from general Institute funds for the basic upkeep of the health service, and this is supplemented by an insurance plan costing $11 per semester. When all the differences in bookkeeping and allowances are calculated, the true cost of the two plans comes out almost exactly the same.

A short time ago (1949) Gossage,[26] of the University of Toronto, made a study of medical insurance and prepaid medical plans in student health services in the United States and Canada. As in other aspects of the field, he found little uniformity in practice among the various colleges. The fees charged for supplementary insurance usually varied from $5 to $10 per semester at that time. Most of the plans allowed for hospital board and care with some limitation, additional hospital services, such as x-ray examination, anesthesia, use of operating room and similar charges, surgical fees based on rates usual in the community, a fee for each visit for a physician while the student is in the hospital, and some allowance for treatment resulting from injury to sound, natural teeth. Practically none of these plans provided for treatment of conditions existing before the insurance was taken out, for office calls or home care, eye refractions or dental work, and most of them had over-all limits of $500. In general the cost has risen considerably since that time for most plans.

Yale University has a plan that covers the cost of illness or injury up to $1,000, the student or his parents paying the next $1,000, after which the insuring agency pays up to a limit of $12,000. This extra catastrophe insurance costs $13 a year.[27]

College Physician and Nurse

The qualities needed by the college physician are much the same as those that are desirable in any setting. As a first requirement, he should have had a good training in a first-class medical school, followed by a good internship. In addition to whatever special training he may have had, it is desirable that he have had some experience in general practice. A reasonably robust physique is needed, for contrary to a considerable body of opinion among physicians, the demands are strenuous. He should not have a "prescription reflex," based on a feeling that he has not done his duty by a patient unless he has given or ordered some medication. He studies the total situation of the student — physical, mental, moral and spiritual. He should think largely in terms of the maintenance of health rather than confining himself to the treatment of disease in his patient. He should like to work with young people and should have confidence in their basic good intentions and in their capacity to learn from experience. If he is irritated by them, students soon sense this fact and will not even appreciate otherwise excellent medical service. Finally, he should believe in the long-term values of what he is doing, precisely as the good teacher does in other departments.

A co-operative relation with many other people in a college community is a necessity, and this is somewhat different from that of the private physi-

cian to people in his community. The college physician is vulnerable to all kinds of criticism, responsible and otherwise, and communication is usually good enough for him to be aware of much of it. He must be able to accept such criticism, adapting it to constructive purposes when possible. Daily exposure to ideas of people trained in such widely different fields as economics, history, science, philosophy and sociology is both rewarding and stimulating. The college physician must be accepted as a person first, and then as a doctor of medicine, if he is to accomplish the maximum of which he is capable.

It cannot be overemphasized that the accomplishments of the college health service are dependent to a major degree on good relations between the physician and the dean and president. Warm support by these officials and by the faculty helps the physician do his best work and in addition is reflected in greater confidence on the part of students. This support is based largely on a respect for ability, which must be earned and deserved.

Whether full-time or part-time medical service by the individual physician is preferable is a moot point; perhaps the full-time arrangement is most satisfactory in colleges that are situated away from medical centers. Conversely, one or more full-time physicians supplemented by varying degrees of part-time assistance by specialists is peculiarly suited to universities near urban medical centers. Even in these institutions, however, it is desirable for the part-time physician to develop a special interest in the problems of the college as a whole.

The position of the nurse in a college health service is a vital one. A good nurse who likes working with young people and who views their many problems and idiosyncrasies with sympathy and humor can do much to improve the quality of medical care given. A college nurse has to be a combination of qualities all of which, if beneficial, are most helpful in helping maintain the student's sense of security. It is not at all uncommon in college infirmaries for students to return, after their recovery, for advice or support in crisis situations. This suggests that the nurse exercises a counseling relation of great value. She helps in interpreting medical care to patients.

National Co-ordination

The national organization that has been most active in the field of promoting health measures of all kinds, particularly those relating to medicine, is the American College Health Association (until 1948, the American Student Health Association). This organization was organized in 1920 and has held annual meetings since that time with the exception of three years during World War II. The last meeting was held in Boston in 1952. Membership is by colleges and the roster consists of about 225 institutions. The organization's purpose is that of raising the standards of health services in colleges, promoting educational measures that tend to bring such improvement and sharing information concerning new projects being carried out in the various colleges. To this end it has co-operated with other organizations that have a strong interest in student health in a series of conferences on health in colleges; three have been held so far, in 1931 at Syracuse University, in 1936 in Washington, D. C., and in 1947 in New York City. The Fourth National Conference on Health in Colleges will be held in New York in May, 1954, when a number of difficult problems confronting the workers in this field will be studied by physicians, health educators, athletic coaches and directors, professors of physical education, deans and college presidents. Among non-college agencies, the National Tuberculosis Association has taken the lead in helping to call attention to the opportunities for health promotion in colleges, not only by major financial support of these conferences but also by imaginative leadership.

After each conference a volume has been issued that reflects as far as possible the desirable standards of college health services. The last volume[28] is a valuable guide for any college administration that wishes to determine whether it is making maximum use of opportunities in this field. A similar volume will be issued by the Fourth Conference, embracing as far as possible the commonly accepted practices and concepts up to 1954.

Recently, the Department of Preventive Medicine at Cornell University has inaugurated a new semi-annual journal,[29] devoted entirely to various aspects of student health. The high quality of the first issue invites widespread support by physicians interested in this field.

Many persons both within the American College Health Association and in other agencies interested in this field are giving much thought to the place of health agencies in an educational institution, and a special committee of the Association is working on a detailed description of functions and standards in this field. From preliminary reports of that committee, headed by Dr. Ralph Canuteson, of the University of Kansas, and from personal experience and observation, is derived the following summary of what aims a college health service should have.

Ideal College Health Service

Objectives

To promote individual and general health in the college community by means of a program of comprehensive medical care.

To prevent illness or injury when possible, in terms not only of sanitation and living conditions but also of factors promoting social and emotional maturity.

To serve as an educational center for the collection and dissemination of information that

affects the health of the community; this includes the maintenance of a referral or consultation service to enable college personnel to make effective use of the medical resources of the community.

To aid in freeing the student or staff member from physical or emotional handicaps that prevent him from utilizing to the fullest extent the academic, extracurricular or environmental resources of the college.

To care for sick students or staff members.

Standards

All college health services should meet minimum standards for practice as specified by supervisory agencies such as the state health departments, the American Medical Association, the American Hospital Association or the American College of Surgeons. The director of a college health service should be a licensed physician directly responsible to the head of the institution, though on many matters he would report to responsible officials acting on behalf of the president.

Relations with Other College Departments

The director and his associates should establish and maintain effective working relations with all other departments in the institution; some departments have frequent and recurring problems whose solution is attained more readily with medical collaboration.

Admissions Office

All entering students as well as those readmitted after a significant absence should have an examination sufficiently thorough to reveal health hazards to the individual or to the community.

Counseling and Other Special Services

An adequate counseling or advising service, especially when broadly based and carried on by many faculty members, inevitably brings to light the presence of seriously disturbed students. In such cases consultation with a physician, a psychiatrist, if one is on the staff, or with a psychologist and the physician if there is not, serves to protect the interests of the student as well as the faculty member.

Dean's Office

The overlapping of problems between a health service and the office of the dean of students is so great and the complications so numerous that almost daily consultation is needed between the two. Officials of both offices need to know the general problems of the other, due care being taken to respect personal confidences at all times and to keep their functions distinct in the minds of students.

Athletics and Physical Education

All students should be cleared by the health service for participation in athletic activity. Only a physician should authorize resumption of activity by an injured student. A physician should be in attendance at all scheduled contests in sports that have more than usual health hazards (body contact) and on call for the others.

Health Education

The practices are so varied in American colleges regarding how to achieve a measure of health education that definitive, uniform procedures are impracticable. The physicians of college health services should consider one of their primary duties to be that of directing sound health practices in safety, sanitation, diet and control of communicable disease or emotional disorders. In some situations this may be done by classroom teaching, either by separate courses or by collaboration with academic departments in courses in physiology, sociology, anthropology, social history, chemistry, engineering, psychology or wherever medical insights may be productive. In others indirect means may be most suitable: individual conferences, occasional seminars, fliers on bulletin boards, health campaigns, articles in student publications, talks to college groups and the hundreds of informal contacts by telephone and in dining rooms.

Faculty

As far as possible, the college physicians should be available for consultation with interested faculty members about general health problems both of their students and of the community.

Summary

Health services in the colleges and universities of the United States and Canada have made important forward strides, especially in the last three decades. Recognition that the health of students and faculty is a matter of importance in an educational sense as well as in a personal one is growing. Accordingly, colleges have attempted to build health in positive ways in addition to attempting to see that students and faculty get the best possible individual medical treatment. These measures include programs of tuberculosis control, immunization against communicable disease, research, mental hygiene, environmental sanitation, safety, prepayment and insurance plans, and co-operation with all other college departments on health matters. Student medicine is not a separate specialty but does call for a special point of view regarding specific problems of a more or less limited age group. In fact, those who enter this field full time are forced by circumstances to go in the opposite direction from specialism to a considerable extent and to become general medical advisers.

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MEDICAL INTELLIGENCE

CONGENITAL AFIBRINOGENEMIA

Report of A Case

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CONGENITAL afibrinogenemia is a rare disease that was first described by Rabe and Salomon[1] in 1920. Since that time about a dozen cases have been reported in the medical literature. A recent report from Ceylon[2] described the occurrence of this disorder in a child of mixed English and Eurasian parentage. Probably other cases have been encountered, although not recorded in the medical literature. Henderson, Donaldson and Scarborough[3] have presented a case and given an excellent review. The most interesting feature of the case discussed below is the fact that the patient, a girl in her twentieth year, seems in excellent health and has menstruated in a normal way since the age of thirteen. So far as I am aware no similar patient has previously been described.

CASE REPORT

A 19-year-old woman, the daughter of Armenian parents, both of whom had been born in the near East, was first seen in April, 1949, when she was 16 years old. She had been born in Rhode Island.

Since early life she had had several episodes of alarming and uncontrollable bleeding from lacerations resulting from childhood accidents. The hemorrhage could not be arrested until she was given transfusions of blood, which on each occasion caused prompt cessation of bleeding. In addition on 2 or more occasions troublesome bleeding had followed extraction of teeth. As noted in other patients with this disorder, however, she had intervals of months or years without trouble of any sort, the hemorrhage occurring only as a result of injuries. She had never had nosebleeds, bleeding gums, hemarthrosis or hematuria. She almost always had several black-and-blue spots on her arms or legs, the result of slight trauma such as bumping against furniture. During the summer she occasionally had troublesome bleeding when she shaved her legs. She enjoyed unusually good health and had an excellent appetite. She was active and athletic.

Catamenia had begun at the age of 13, and the menstrual periods were very regular. There was no flowing or staining between periods, nor had there been any excessive flowing in the 6 or 7 years since the onset of the menses, except for a single occasion in the summer of 1948, when profuse flowing occurred on the 1st day of a period. This experience had never been repeated.

The patient had had most of the common diseases of childhood, apparently without complications, although as an infant she had had an attack of pneumonia during which the was very seriously ill. She had never had any surgical operations. She graduated from high school in 1950 and was regularly employed, rarely, if ever, losing time from work because of any disturbance in her health.

The family history was of interest. There was no consanguinity of the parents (a situation that has been reported as common in other cases of this disease). A brother had died 3 days after birth as a result of uncontrollable hemorrhage from the umbilical cord. The patient's mother had a history of easy bruising throughout her life but had never had any serious hemorrhage. Examination of her blood revealed a mild deficiency in fibrinogen (150 mg. per 100 cc.). The patient's father, a brother and a sister were living and well, with no evidence of a hemorrhagic tendency.

Physical examination was almost entirely negative. She was well developed and well nourished; she had excellent color. No abnormalities were noted except 2 carious teeth and the presence of several ecchymotic areas on the outer aspect of both arms and legs, most of which she was able to attribute definitely to bumping into some object. She appeared on the whole to be a normal, cheerful and healthy girl.

Laboratory examinations were negative except for the complete incoagulability of the blood. There was no evidence of anemia, the red-cell count, hemoglobin and hematocrit being within normal range. The white-cell count and differential count were normal, and there was no deficiency of

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platelets. The bleeding time was variable — on one occasion being somewhat prolonged. Blood samples taken at the time of the first visit were observed for as long as 3 days, during which they remained completely incoagulable. The addition of thrombin produced no clot or precipitate. Heating plasma to 60°C. produced no precipitate or opacity. Because of the complete absence of clotting and in view of the personal and family history a provisional diagnosis of congenital afibrinogenemia was made.

Through the kindness of Drs. William B. Castle and Walter Frommeyer, Jr., of the Thorndike Laboratory at the Boston City Hospital, the complete absence of fibrinogen was confirmed. Later, through the kindness of Drs. John T. Edsall and Douglas Surgenor, of the Laboratory of Physical Chemistry at Harvard, the electrophoretic pattern of the blood plasma was determined; the absence of a pattern for fibrinogen provided additional confirmation of the diagnosis. The specimens of blood examined on these occasions were obtained during a menstrual period and on the last day of and the day after a menstrual period. These times were chosen particularly because it had been suggested that the absence of excessive flowing at the time of menstruation might be due to the temporary production of sufficient fibrinogen to prevent hemorrhage.

Examination of the blood showed a red-cell count of 4,390,000, with a hemoglobin of 12.4 gm. per 100 cc. and a hematocrit of 40 per cent, and a white-cell count of 5100, with 60 per cent neutrophils, 2.5 per cent eosinophils, 0.5 per cent basophils, 29 per cent lymphocytes and 8 per cent monocytes. The blood platelets were 260,000, and the sedimentation rate less than 1 mm. in 1 hour. Examination of a stained blood film showed the red cells to be uniform in size and shape except for an occasional oval or pencil form. There were no abnormal forms of white blood cells. Platelets appeared to be present in normal numbers. The bleeding time was 7 minutes; there was no coagulation after 3 days.

Table 1. *Measurement of Clotting Time.*

Portion of Plasma Mixture		Recalcification Time
Patient's plasma	Normal plasma	
%	%	*sec.*
0	100	90
20	80	85
33	66	90
50	50	85
80	20	85
100	0	3600+

Blood Wassermann and Kahn tests were negative, as was urinalysis.

Since the patient's whole blood failed to coagulate in 24 hours, several special blood tests were performed* to determine the nature of the coagulation defect. On mixing of equal portions of the patient's oxalated plasma and 7.5 per cent thrombin solution, no clot ensued. This indicated either that fibrinogen was absent or that a powerful anticoagulant was present. The possible presence of an anticoagulant was investigated by measurement of the clotting time on recalcification of the oxalated plasma of the patient mixed with normal oxalated plasma in varying proportions (method of Quick). The results of these measurements are presented in Table 1. It was apparent that the recalcification time was not increased when the patient's plasma constituted a large fraction of the total plasma mixture, and that a potent anticoagulant was therefore not present.

In the 1-stage prothrombin determination (method of Quick) no clot followed the addition of thromboplastin and calcium chloride to the patient's oxalated plasma. However, if 2 per cent fibrinogen solution was added to the plasma before the test was performed, clotting occurred in 15 seconds. Normal plasma similarly treated also clotted in 15 seconds. With the prothrombin test of Rosenfeld and Tuft, in which prothrombin-free normal human plasma is used to dilute the patient's plasma, the concentration of prothrombin was 105 per cent of normal. Here, the fibrinogen was furnished by the diluent. These observations indicated that clotting readily occurred if fibrinogen was added to the system and that the concentration of prothrombin and the rate of prothrombin conversion to thrombin were both normal in the patient's plasma. Thrombin was also demonstrable in the patient's whole blood 19 minutes after venesection. Although quite fluid at this time it rapidly (in 3 minutes) clotted added fibrinogen.

The residual serum prothrombin was measured in whole blood after 24 hours at 37.5°C. Whether or not fibrinogen had been introduced into the system, the residual prothrombin was 5 per cent or less, a normal observation. Since the clots produced by addition of fibrinogen did not undergo lysis on prolonged incubation, no abnormal fibrinolysin was present in the patient's plasma. Clot retraction was observed to be normal within 1 hour when 0.2 cc. of 2 per cent fibrinogen solution was added to 2 cc. of whole blood.

In August, 1950, electrophoretic partition of the patient's plasma proteins was effected by Drs. John T. Edsall and Douglas Surgenor. There were normal concentrations of the several components of the plasma proteins, with the exception of the total absence of a pattern characteristic of fibrinogen (Table 2).

Table 2. *Results of Electrophoretic Partition.*

Type of Protein		Percentage of Total Protein
Albumin		64
Globulin	Alpha	15
	Beta	10
	Gamma	7
	Fibrinogen	0

Blood studies on the mother of the patient demonstrated the following values: clotting time, 8 minutes; prothrombin time, 15 seconds; prothrombin concentration, 105 per cent; fibrinogen, 150.5 mg. per 100 cc.; circulating anticoagulant, 0; prothrombin consumption, 5 per cent residual prothrombin; hemoglobin, 13.1 gm. per 100 cc.; and hematocrit, 41 per cent. Fibrinolysis was absent.

Discussion

As stated above this case was of unusual interest because of the fact that menstruation was entirely normal. It clearly demonstrated that a normal menstrual flow is possible despite the inability to form a fibrin clot.

This young woman illustrates in a striking manner the indispensable role that complete vascular integrity plays in protecting her from continued troublesome hemorrhage. Probably her youthful, healthy tissues, with normal elasticity, are her present salvation and, because of normal platelets and vasoconstriction, serve to protect her in spite of this serious defect in coagulation. The blood vessels of the uterus are distinguished by the marked tortuosity of the coiled spiral arteries that slows the rate of blood flow in the endometrium; these arterioles also exhibit unusual vasoconstrictor activity.

Markee[4] has made a fascinating study of the changes in the endometrium during menstruation by means of transplanting bits of endometrium into the anterior chamber of the eye in monkeys. His account provides an excellent illustration of the

*By Dr. Walter Frommeyer, Jr.

remarkable vasomotor activity and the beautiful precision of the orderly sequence of changes that occur in the endometrial vessels under humoral influences and that regulate and control menstrual flow.

What the future may bring about cannot be predicted. Certainly, any condition that impairs vascular integrity will cause trouble. Lack of vitamin C or platelet deficiency, whether primary or symptomatic, would result in serious hemorrhage. Similarly, infections, toxins or any inflammatory processes that cause vascular damage would be dangerous. Ovulation, which probably occurs regularly, has to date caused no trouble, though this is also a potential source of danger. Vascular degeneration as the patient grows older will again be a threat to her. If she survives long enough for such a degeneration of vessels to occur it may be necessary or wise to give an intravenous injection of fibrinogen at regular intervals. Experience with this girl so far has shown that a single transfusion of 500 cc. of whole blood will cause the arrest of hemorrhage, and on one occasion permitted the extraction of 2 teeth with complete safety. A single transfusion of 500 cc. of whole blood would produce a level of fibrinogen in the circulating blood below the normal level of 250 to 400 mg. per 100 cc., but to date it has always provided enough fibrinogen to permit the formation of a firm fibrin clot and the arrest of hemorrhage. Fortunately there appears to be no tendency to the development of a refractory state, which has frequently occurred in hemophiliac patients who have been given repeated transfusions of blood or plasma, particularly of the so-called antihemophilic globulin.

A very difficult problem for this patient is certain to arise in the near future. Since she is otherwise in excellent general health and is, in addition, a vivacious and attractive girl, it is almost certain that some young man will fall in love with her, and the question of the advisability of marriage and childbearing will arise to plague her and the doctors who must attempt to give her sound advice. Two considerations are involved in this problem: the safety and welfare of the patient, and the possibility of inheritance of this serious disease by any children she might have. In this case there is a strong familial tendency, as shown by the partial deficiency of fibrinogen in the mother, and the probability of complete afibrinogenemia in a brother, 1 of 3 siblings.

Summary

A case of afibrinogenemia in a young woman in her twentieth year is described.

Partial deficiency of fibrinogen was found in the patient's mother. A brother died of hemorrhage from the umbilical cord about a week after birth.

In spite of the absence of fibrinogen and the consequent complete incoagulability of the blood, the patient has had normal menstruation for six or seven years. She has long periods of complete freedom from symptoms and no residual disabilities, in contrast to patients with hemophilia.

Since this report was prepared I have received a communication from Dr. H. H. MacKinnon, of Fredericton, New Brunswick, giving details of a patient observed by him in March, 1951. The patient was a twenty-year-old woman who had a history of prolonged bleeding after slight trauma throughout her life. She had, however, no excessive bleeding with menstrual periods. Blood studies revealed a complete absence of fibrinogen. This was considered to be a case of congenital afibrinogenemia.

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BY THE LONDON POST

Foundation of the British Museum — Main Drainage of London — Putting the Patient at Ease

John Lister, M.D.

London, England

THE British Museum and the Natural History Museum this year commemorate the bicentenary of their foundation, but I doubt whether it is generally known that these museums came into being as the direct result of the will of an eminent physician and naturalist, Sir Hans Sloane. G. R. de Beer, F.R.S., director of the Natural History branch, recently described in a leading article in the *Times*, how this came about.

Born in Ireland in 1660, Sloane came to London at the age of nineteen to study medicine. There he met the chemist and physicist Robert Boyle, and in 1683 he set out on the grand tour of France that was then usual for all aspiring British medical students. On returning to London in 1684, he was introduced to medical practice by Sydenham. A year later he was elected a fellow of the Royal Society, and shortly afterward he accepted the post of physician to the Duke of Albermarle, who was then governor of Jamaica. In that island Sloane made an intense study of natural history and made the hobby of collecting, his method of advancing knowledge. He returned to England in 1689 and took his place among the men of science. In 1695 he married the widow of a Jamaican sugar planter and took a house in the fashionable suburb of Bloomsbury. There he amassed his collection of plants, animals, fossils, manuscripts and works of art. There too he entertained his friends, who included Isaac Newton, Samuel Pepys, Christopher

Wren and many others. He corresponded with leading men overseas and among the eminent foreign visitors who came to see his museum were Benjamin Franklin, Voltaire and Handel, the last of whom disgraced himself by putting a buttered muffin down on a precious book.

As a physician, Sloane helped to introduce the scientific method of experiment into medicine, and he is the only man who ever held the post of president of the Royal College of Physicians and that of president of the Royal Society (he succeeded to the latter on the death of Newton).

Sloane lived to the great age of ninety-two and spent the last years of his life in arranging his vast collections and in making codicils to his will for their disposal after his death. He wanted them to be kept together and made accessible to students for the advancement of learning to all posterity. He therefore proposed that the nation should buy his collections from his daughter for £20,000 and make them into a national museum. After his death, Parliament agreed to carry out his will, and that is why this year is the bicentenary of the foundation of the British Museum and its sister, the British Museum (Natural History).

Main Drainage of London

The chief engineer of London County Council recently gave an interesting lecture on the main drainage of London. He recalled that the necessity for drainage had been recognized from early times and that there were records of sewers at Nineveh three thousand years ago and of an elaborate drainage system at the palace of Minos in Crete in the year 2000 B.C.

In the Middle Ages, there was a general deterioration of sanitary standards, and in London the earlier sewers were natural watercourses, in particular the Kilburn, Westbourn, Fleet and Shoreditch, north of the Thames, and the Effra and Ravensbourn on the South. The Bill of Sewers was passed in the reign of Henry VIII, and under it commissioners of sewers were appointed with power to levy rates and carry out useful works.

In the nineteenth century, when three alarming outbreaks of cholera were thought to be due to bad drainage, many London houses still had no drains, and most of those that were drained had overflowing cesspools beneath them. With the growth of piped water supplies, the Commissioners gave permission for waterclosets to be connected to the sewers, and in 1847 this was made compulsory. A difficulty in maintaining constantly efficient drainage was the fact that the outfall of the streams and sewers was below the level of high tide in the Thames, and it was not until 1874 that a drainage system overcoming this problem was completed. Intercepting sewers running parallel to the river were provided, and the flow was concentrated at two eastern outfalls on the North and South bank of the Thames, where huge reservoirs were constructed, in which the sewage was stored during flood tide and discharged into the estuary at ebb.

At the present time, there are beneath the streets of the County of London about 2750 miles of local sewers maintained by Borough Councils and the Corporation of the City, and over 400 miles of much larger mains and intercepting sewers, which are the concern of the County Council. The annual cost to the ratepayer is £935,000, or just over 4 shillings per head of population.

In conclusion, the lecturer mentioned two special difficulties that face the sewage engineer today: the gradual subsidence of the land in South-East England and the surges of the North Sea, which occasionally cause exceptionally high tides in the Thames. The latter point is of great topical interest, for the catastrophic floods that we have just experienced and that affected the lower Thames worse than anywhere were due to this very combination of meteorologic conditions.

Putting the Patient at Ease

Great interest has been aroused both in the lay and in the medical press by a document that the Ministry of Health has just issued entitled "The Reception and Welfare of In-Patients in Hospital." This memorandum calls upon doctors and nurses to remember that the sick person is an individual and not a "case" and warns them that "it is difficult for those familiar with hospital life to realise just how incomprehensible and alarming hospital routine appears to the outsider."

Starting with the patient's admission to the hospital, the report considers nearly every conceivable aspect of hospital life from his point of view. On arrival at the hospital, he should not be left to find his own way to the ward along confusing corridors, but should be directed by a receptionist as in a hotel. The ward routine should be as flexible as possible. Visiting times should be generous, and great importance should be attached to the quality and serving of meals. The reduction of all unnecessary noise is urged, and to this end it is suggested that earphones and pillow telephones replace radio loudspeakers and that ward trolleys always be fitted with silent wheels.

Concerning the use of patients for teaching purposes, the report states that "the welfare of the patient must never be subordinated to the needs of teaching," and the *Lancet*, in considering this point, deprecates the still strangely prevalent habit of discussing the patient's more alarming symptoms across his bed with a group of students. The *Lancet* also condemns the teacher who withdraws a short distance and says in a penetrating whisper: "Of course, we can't say when the next catastrophe will come: it may be in six years — or six days."

Although there are many hospitals in which most of the recommendations of this memorandum are already well established, there are others where much could be done to make the patient happier. The *Times* concludes its remarks on the subject by urging that "there should be no delay in seeing that the general standard is raised to the level of the best."

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 39131

PRESENTATION OF CASE

A forty-four-year-old woman entered the hospital because of jaundice of three months' duration.

Fifteen months before admission the patient consulted her physician because of obesity, her weight being 190 pounds. A basal metabolic rate was found to be −12 per cent, and she was placed on thyroid, 0.06 gm. (1 gr.) daily. About twelve months before entry generalized pruritus, apparently without jaundice, developed, persisting to the time of entry. Five months before admission for several weeks she experienced easy fatigability unassociated with nausea, vomiting, fever or any other symptoms. Two months later she noted the onset of painless jaundice, not immediately preceded by an acute illness or subsequent increase in pruritus. For the past month she had observed that her urine was dark amber and thought that stools were somewhat lighter than usual. During this period she began to have sharp pains, "like bee-stings," in the middle three fingers of each hand, and later this sensation was noted at both elbows and knees. About this time her physician prescribed a fat-free diet, which she followed faithfully. Since taking thyroid she had gradually lost 25 pounds. Her appetite was good, and her diet was adequate. During this fifteen-month period she had never had any bouts of chills, fever, or abdominal pain, and there was no history of indigestion or intolerance to fatty or greasy foods. Her bowels moved more easily, but stools were no more frequent or bulky than usual and not foul smelling or fatty. She drank 10 cups of coffee, smoked about 30 cigarettes daily, and had 3 or 4 highballs a week. There was no known exposure to chemical solvents or other toxic substances.

The past history revealed that at the age of ten the patient had jaundice "for a long time." Eight years before admission fever and generalized abdominal pain suddenly developed, lasting for two weeks, after which the pain subsided but low-grade fever and "a high white-cell count, around 40,000," persisted for a year. This did not interfere with normal activity. About a year after the fever subsided she again had an acute episode of abdominal pain, fever and leukocytosis. An exploratory laparotomy at that time was negative, and symptoms subsided after ten days of sulfonamide therapy.

Physical examination revealed a moderately icteric woman with liver-colored palms. There were two spider angiomas over the upper sternum and a questionable spider angioma on the right cheek. Over both elbows and all fingers there were minute yellowish papules, with discomfort to pressure over the middle three fingers of both hands and both elbows and knees. The submaxillary lymph nodes were slightly enlarged but soft and freely movable. Examination of the chest, heart and abdomen was negative.

The urine was dark amber and acid, had a specific gravity of 1.026 and gave a ++ reaction for bile; the sediment contained rare red cells, 5 white cells and 20 epithelial cells per high-power field. The urinary urobilinogen was present in a dilution of 1:200. Examination of the blood revealed a hemoglobin of 11.5 gm. per 100 cc. and a white-cell count of 9700, with 57 per cent neutrophils, 26 per cent lymphocytes, 12 per cent monocytes and 5 per cent eosinophils. The icteric index was 35, the prothrombin time 20 seconds (normal, 18 seconds) and the cephalin flocculation ++ in twenty-four and ++++ in forty-eight hours. The serum bilirubin was 4.80 mg. direct and 6.85 mg. total, the alkaline phosphatase 75.4 Bodansky units, the phosphorus 3.1 mg., the nonprotein nitrogen 25 mg., the total protein 7.24 gm., the albumin 4.07 gm., the globulin 3.17 gm., the cholesterol 1115 mg., and the cholesterol esters 485 mg. per 100 cc. On two occasions the serum was found to be too fatty for vitamin A and carotenoid determinations. A glucose tolerance test was reported as 102 mg. per 100 cc. fasting, with a rise to 127 mg. at half an hour and a drop to 102 mg. at two hours. The blood Hinton test was negative. A stool specimen was brown, guaiac negative, ++ for bile and negative for fat. Duodenal drainage showed an increased number of cholesterol crystals but no bile-stained white cells or bilirubin crystals. A basal metabolic

rate was +19 per cent. A Graham test was reported as negative except that there was less concentration of the dye than was usually seen. There were no stones.

In the hospital the patient's condition remained unchanged, and on the sixteenth hospital day an operation was performed.

Differential Diagnosis

Dr. Charles S. Davidson*: To put a name to the diagnosis in this case is, I think, relatively simple. The patient had xanthomatous biliary cirrhosis, a disease that occurs usually in women between the ages of thirty and sixty and is characterized by jaundice of long duration, dark urine, always pruritus, hepatomegaly and small xanthomas usually scattered widely over the body. The onset is insidious, and the course is progressive and prolonged. The serum lipids are markedly elevated, producing xanthelasma and xanthomas. The elevated serum lipids are characteristically cholesterol, the phospholipids and neutral fats; also, the serum is usually clear, presumably because the neutral fat is well "stabilized" by the phospholipids. The striking elevation of serum alkaline phosphatase–75.4 Bodansky units — is also characteristic of the disease. Spider angiomas and palmar erythema are commonly seen. The curious condition from which this patient suffered, therefore, is quite characteristic of the disease known as xanthomatous biliary cirrhosis.

I might sit down now, having made the diagnosis, and perhaps I should, since further inquiry into the nature of this disease is not as easy as naming it. Putting a label to the signs and symptoms, which is easy to do, is like saying that a patient with asthenia, brownish pigmentation, hyponatremia, delayed water tolerance and so forth has Addison's disease without consideration of the pathologic physiology of the condition. I must decide why this patient had this strange disease, and that is where I get into trouble.

This disease was recently discussed by Dr. Keith Gray,[1] of Mt. Lawley, Western Australia, who notes that it was first described a hundred years ago from Guys Hospital by Addison and Gull.[2] A young woman, aged thirty-three years, with the interesting name of Eliza Parachute, attributed her condition to fright and to a blow received in the left groin while she was attempting to separate two men who were fighting. Two days after she received the blow, she became jaundiced and had pain in the hypochondrium and itching; the jaundice persisted, and xanthomatous plaques appeared.

It is perhaps unfortunate that this condition has been named because it can arise from two importantly separate phenomena, intrahepatic and extrahepatic biliary obstruction. That is, jaundice may be due to parenchymal liver disease or to extrahepatic obstruction. This problem, which comes up every day on the wards and regularly at clinicopathological conferences, is the same in the case under discussion.

As far as I know, xanthomatous biliary cirrhosis, whether primarily intrahepatic or arising from extrahepatic obstruction, has an almost identical clinical picture so that it is difficult to distinguish the two. It may follow atresia of the bile ducts in children and stones in the common duct, or carcinoma of the ampulla or head of the pancreas in adults — in other words, the condition may arise from any long-standing biliary obstruction, usually not complete but partial. The intrahepatic concept of the disease was originally popularized by Thannhauser.[3] He thought it was a primary disturbance of the fat metabolism, with secondary deposition of fat in the liver and biliary radicles, and a secondary reaction around the fat, with obstruction and the appearance of jaundice and liver disease on that basis. This sequence of events probably does not occur, or is rare if it does. It appears more likely that the primary liver disease is due to damage of bile canaliculi from other causes than fat deposition. This may be and probably is most commonly idiopathic or may occasionally follow trauma, as it did with Eliza Parachute. It also follows, as Hanger and Gutman[4] have shown quite clearly, the administration of arsenicals; some of the cases of hepatitis that follow arsenic are probably on this basis and not due to serum hepatitis. Thirdly, it can arise as a complication of infectious hepatitis. In an excellent article, which has been extensively discussed, Watson and Hoffbauer[5] describe a syndrome following upon infectious hepatitis that they call cholangiolitic hepatitis. They describe typical infectious hepatitis progressing into chronic hepatitis, with chronic jaundice, and on examination of the liver the cholangioles are found to have disappeared. In none of their cases was xanthomatosis described; however, the serum cholesterol was often elevated, sometimes rather markedly although not to as great an extent as in the case under discussion. One of their patients closely resembled the one under discussion in that she was about the same age and had had hepatitis many years before the symptoms appeared and then some years later the appearance of cholangiolitic cirrhosis.

How can we distinguish intrahepatic from extrahepatic disease in this patient? With the few hints given I could build up a case for either side without difficulty. In the first place the patient had something at the age of ten years that sounds very much like infectious hepatitis. Secondly, she had at least two episodes, eight and six years before admission, of abdominal pain, fever and leukocytosis that may have been due to stone, or to some intra-abdominal phenomenon unrelated to this disease. These symptoms do not sound like recurrent hepatitis to

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me although the patient of Watson and Hoffbauer[5] mentioned above had a similar occurrence some years after the original hepatitis. Thirdly, in favor of the intrahepatic obstruction is the gradual onset, with pruritus and jaundice — not an acute but a gradually progressive course. The marked evidence of liver disease (++++ cephalin flocculation and the increased urinary urobilinogen) further lead me to lean to intrahepatic etiology. The negative exploratory laparotomy worries me on all counts; particularly, there should have been evidence of intrahepatic disease at that time. However, intrahepatic disease can appear minimal on gross examination, and presumably no biopsy was done; certainly it was not reported to us. These are the factors that I believe are in favor of intrahepatic obstruction.

I can also build a good case for extrahepatic obstruction. The abdominal pain may have been related to the passage of a stone or to some other extrahepatic blockage in the larger bile radicles. The normal prothrombin time, the normal albumin and the fact that the cholesterol esters were not more reduced than they were with the very high total cholesterol make necessary serious consideration of extrahepatic obstruction. These two types of obstruction are almost indistinguishable as far as I can tell.

There have been a number of excellent reviews of this subject that I might mention. The group at the Rockefeller Hospital[6] point out the close resemblance of intrahepatic and extrahepatic obstruction and note that the high blood fat and appearance of xanthomas are intimately related as one might expect but bear no relation to whether the disease is intrahepatic or extrahepatic — that is, if the disease goes on long enough and if the blood cholesterol and phospholipids rise sufficiently, xanthelasma and xanthomas will appear whether the disease is intrahepatic or extrahepatic. Recently, there have been a number of articles on this subject, particularly those of MacMahon and Thannhauser,[7] Shay and Harris,[8] Hanger[4] and Bevans and Batchelor.[9]

Because it is difficult to distinguish between extrahepatic and intrahepatic disease, every patient who has this condition certainly should be explored, and this patient was.

I should favor a diagnosis of primary intrahepatic biliary cirrhosis (cholangiolitic cirrhosis or cholangiolitic hepatitis) due to old infectious hepatitis, perhaps with exacerbations and with cholangiolitic fibrosis, resulting in hypercholesterolemia, hyperlipemia and the appearance of xanthomas. There is the possibility that pancreatitis was also present.

DR. CHESTER M. JONES: Dr. Davidson, do you think it is surprising, in view of the whole story, that the patient did not have a demonstrably palpable liver or spleen?

DR. DAVIDSON: I certainly do; there should have been a very large liver. That did worry me, and I should have mentioned it. Also I should have mentioned that all high blood fats are not due to biliary cirrhosis; they can occur in a great many other conditions, — idiopathic, diabetes and so forth, — but not with jaundice and evidence of hepatic disease.

A PHYSICIAN: I wonder if you could tell us what the reticulocyte count was?

DR. JONES: The reticulocyte count was not done because we thought that this was not a hemolytic type of jaundice.

A PHYSICIAN: Were phospholipids determined?

DR. JONES: Phospholipids were not determined because it was impossible to get them.

A PHYSICIAN: Did the serum look fatty?

DR. DAVIDSON: I, too, should like to know whether the serum looked fatty or was clear.

DR. JONES: I cannot find any mention of that here although somebody must have noted it at the time.

DR. EDGAR B. TAFT: The only thing I find mentioned is that a vitamin A determination was not done because the serum was too fatty.

DR. PERRY J. CULVER: I wonder if the presence of excessive fat, unless it clouds the serum, interferes with a vitamin A determination.

DR. DAVIDSON: I looked that up; the serum has to be specially handled, and if it is very fatty, it has to be extracted.

CLINICAL DIAGNOSIS

Xanthomatous biliary cirrhosis.

DR. CHARLES S. DAVIDSON'S DIAGNOSIS

Primary intrahepatic biliary cirrhosis, with cholangiolitis, fibrosis, hypercholesterolemia and xanthomatosis.

ANATOMICAL DIAGNOSES

Biliary cirrhosis, primary, intrahepatic, with esophageal varices, fibrocongestive splenomegaly and (jaundice).

Pulmonary congestion and edema.

Osteoporosis.

PATHOLOGICAL DISCUSSION

DR. TAFT: The operation mentioned in the protocol was a punch biopsy of the liver, on which we made a diagnosis of acute hepatitis. The clinicians were not at all satisfied with the report so they operated on this patient anyway, removed a wedge of liver and a lymph node, and inserted a T tube into the common duct, which was not obstructed. They also noted that the gall bladder did not appear unusual. On this second specimen we made a diagnosis of biliary cirrhosis, consistent with the intrahepatic type. There was some increase of connective tissue in the portal areas, with bile-duct proliferation and infiltration of polymorphonuclear leukocytes. I should like to point out that it is a favorite saying of Dr. Frederic Parker, Jr., at the Mallory Institute

of Pathology at the Boston City Hospital, that sometimes it is difficult to differentiate microscopically acute hepatitis from early biliary cirrhosis; I think this fact was probably the reason for the two divergent diagnoses. Dr. Benson will give the rest of the history on this patient.

DR. JOHN A. BENSON, JR.: I should like to summarize briefly about 13 admissions.

Table 1 shows the changes in the clinical and laboratory findings during these six and a half years. The nearly complete relief from itching after the first laparotomy was the most dramatic that the patient experienced in her subsequent six-and-one-half year course. A cholangiogram demonstrated no external biliary-tract obstruction, and gradually the T-tube drainage increased to 8 oz. (240 cc.) daily. Nevertheless, although the stools remained brown the jaundice increased as the drainage diminished to only 2 oz. (60 cc.) daily. Three months postoperatively, even though another cholangiogram was normal, the T tube seemed to be serving little useful function since the jaundice, liver size, alkaline phosphatase and cholesterol had increased; therefore, it was removed. She was treated with restricted activity, a high-protein, high-carbohydrate, low-fat diet, bile salts, vitamin K and choline. The last seemed to lessen the recurrent itching, and generally she improved. Seven months after the operation clear-cut xanthomas were diagnosed for the first time.

In the ensuing months she did quite well, with good strength, an excellent appetite, no fever, brown stools and maintenance of weight, serum albumin, and hemoglobin. On the other hand, the cholesterol crept up to 1328 mg. per 100 cc. as the xanthomas multiplied and became tender (Table 1). Jaundice and itching had again become intense. Another punch biopsy revealed unimproved biliary cirrhosis. Therefore, a second choledochostomy and institution of drainage were performed fourteen months after the first laparotomy to relieve the itching. The gall bladder and common duct appeared normal, but there was detritus in the thick mucoid bile and a few tiny crystals were washed out of the hepatic ducts. Liver biopsy was suggestive of a somewhat more advanced process. Coliform organisms were cultured from bile obtained at operation, but two weeks of streptomycin therapy failed to sterilize it. Again, even though there was no demonstrable block there was a striking relief from itching, and the favorable chemical changes shown in Table 1. The jaundice nearly disappeared.

The next fourteen months of the course were perhaps the best. The tube drained well fairly consistently. Spider angiomas faded, and the xanthomas largely disappeared. The serum proteins remained normal. Nine months after the second choledochostomy the patient resumed halftime responsibilities at school.

About four months later, intermittent stoppage of the tube began. A cholangiogram was normal, but the drainage was loaded with calcium bilirubinate. Stool color, jaundice, cholesterol and alkaline phosphatase fluctuated considerably. But itching did not recur for some nine months, when the cholesterol had reached 1020 mg. and the phosphatase 53 units per 100 cc. Stool urobilinogen was considerably reduced. When the T tube was "dry" for any period, the finger joints ached. This all culminated in removal of the T tube in 1948, twenty-two months after its insertion during the first episode of frank cholangiolitis (Table 1).

Again itching became severe, and the xanthomas increased. Although her strength remained good and she was working part time, the patient became depressed. Osteoporosis, with a confining low-back pain, had ensued. Seven months later, a third T tube was placed in the now thickened common duct. Six months later she was better, working some and suffering only minimal itching even though the bilirubin, cholesterol and alkaline phosphatase had again risen to very high levels. The T tube drained only about 6 oz. (180 cc.) daily, but the stools remained brown.

The next year was marked by repeated bouts of cholangitis and by liver decompensation. The liver was enlarging, and the splenomegaly, absent for the preceding two years, had returned. Edema re-

TABLE 1. *Clinical and Laboratory Data during Various Admissions.*

PERIOD	ENLARGEMENT OF LIVER	ENLARGEMENT OF SPLEEN	SERUM ALBUMIN gm./100 cc.	SERUM GLOBULIN gm./100 cc.	SERUM BILIRUBIN mg./100 cc.	PROTHROMBIN TIME sec.	CEPHALIN FLOCCULATION	ALKALINE PHOSPHATASE unit/100 cc.	SERUM CHOLESTEROL mg./100 cc.	COLOR OF STOOL
1945:										
Before choledochostomy	+	+	4.1	4.2	6.9	20	++++	75.0	1115	Brown
After choledochostomy	+	0	5.1	2.5	3.4	19	++	43.0	266	Yellow
1946:										
Before choledochostomy	++	+	4.1	3.7	9.1	22	++++	52.0	1328	Yellow
After choledochostomy	++	+	5.5	2.8	1.8	24	++++	11.5	370	Brown
1948	++	+	3.9	4.0	15.5	20	++++	40.0	496	Brown
1950	+++	+	3.3	4.9	21.0			100.0	275	Brown
1951	+++	++	2.7	3.1	16.4	23	+++	59.2	274	Tan
1952	+++++	+++	3.0	3.7	18.4	14		36.5	548	Tan

appeared after over five years' absence. The patient lost weight. Aureomycin seemed to lessen the mild fever and increase the tube's diminishing drainage. In 1950 the xanthomas and less elevated serum cholesterol were relatively static, and pruritus was not too troublesome (Table 1).

Five years and three months after the first laparotomy esophageal varices were first demonstrated by x-ray examination. At that time bleeding had reduced the hemoglobin to 4.7 gm. per 100 cc. Stool guaiac tests had demonstrated intermittent bleeding for some five years. The prothrombin time had been maintained with oral administration of vitamin K all along. In 1951 transfusions and intravenous injections of albumin corrected this anemia and concurrent ascites and edema, but despite bed rest and hematinics at intervals, the anemia recurred in three months (Table 1). The T tube then drained only a few teaspoonfuls, and

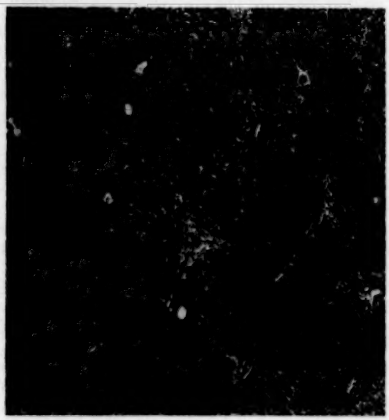

FIGURE 1.

the stools had become light tan. Intermittent courses of chloramphenicol kept the patient relatively afebrile during this year. The jaundice had become green, but her condition was relatively stable.

Six years after the first laparotomy, the third T tube had blocked completely, thirty months after its insertion, and itching was again intense. The tube was therefore removed.

The last six months of her life were spent in a vegetative existence bordering on liver failure despite conscientious nutritional supplementation. Symptoms and signs of parenchymal disease predominated over those of the persistent obstruction in 1952 (Table 1). She acquired a mild upper respiratory infection, and hepatic coma rapidly intervened. Death occurred eight years from the onset of the itching and seven years after the first episode of jaundice.

DR. TAFT: At autopsy the patient was still somewhat obese and was markedly icteric. The liver was extremely large; it weighed 5000 gm. It had a moderately nodular surface, although the nodules were not very large. It was deeply bile stained and green brown. There was some thickening of the capsule. The intrahepatic bile ducts were somewhat thick walled and slightly dilated but not remarkably so. The extrahepatic ducts were similar, and no point of obstruction was found. The gall bladder

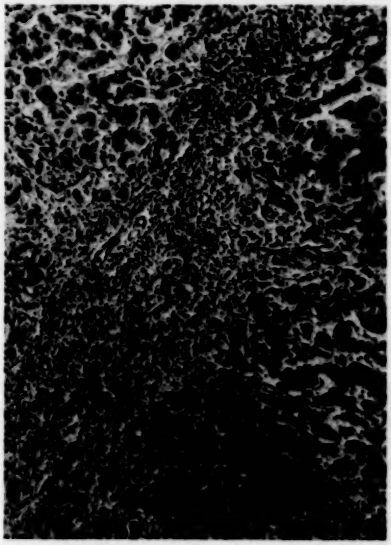

FIGURE 2.

was quite unremarkable. On the cut section, the lobular pattern of the liver in most of the organ was hardly more than slightly accentuated.

I think it is quite surprising, in studying the slides from this liver, — we had six biopsies and the postmortem sections, — that there was only a moderate increase in the fibrosis over seven years of hospital admissions. Figure 1 is from the second biopsy, taken during the first laparotomy. One can see that there is more than the usual amount of periportal connective tissue; occasionally, the fibrous tissue extends between two portal areas. Under

higher power the portal areas are moderately infiltrated with round cells and some polymorphonuclear leukocytes; occasionally, the infiltration exudate extends into the lobules somewhat in the way that it does in hepatitis. There is minimal proliferation of bile ducts. In Figure 2, from the biopsy two years later, there is perhaps more connective tissue than was visible in the previous slide; however, one could find areas in the first slide where there was as much as this. There is more inflammatory exudate and bile stasis in this particular biopsy.

FIGURE 3.

Figure 3 is from the autopsy specimen; actually the amount of fibrous tissue, bile stasis and infiltration of inflammatory cells is not too different from that in the biopsy taken four years before death.

In view of these findings, the evidence of increase in pressure of the portal venous system is somewhat surprising. There were easily demonstrable esophageal varices but no evidence of recent bleeding. The spleen was enormous; it weighed 1700 gm. I am surprised that it was only +++ palpable. I should have thought it was somewhat larger than that.

Since biliary cirrhosis is more often a secondary manifestation of extrahepatic obstruction of the bile ducts, the patients usually die of the primary disease before portal-vein obstruction ensues. Moschcowitz[10] found only 5 cases in a series of 37 adults with extrahepatic biliary obstruction in which there was evidence of long-standing portal obstruction. In 6 additional cases of "primary chronic cholangiolitic biliary cirrhosis," 5 of which were similar in many respects to the case under discussion, 4 had congestive splenomegaly and esophageal varices, and 3 of these patients died of gastrointestinal hemorrhage. It appears, therefore, that increased portal-vein pressure may be a usual complication of this disease.

In addition to the changes in the liver and portal-vein system there was pulmonary congestion and edema, as might have been expected, but no evidence of pneumonia. There was likewise marked osteoporosis, which had been found clinically by x-ray examination.

DR. JONES: There was one interesting feature in this patient that characterizes this group to my mind — the episode of chills and fever a year before death, while the patient was out of this country, was quickly controlled by chloramphenicol. The interesting point was that before the attack occurred there was practically no bile drainage from the in-lying T tube; after chloramphenicol treatment the amount of bile increased until she was excreting about 300 cc. of bile a day for the entire time that she was on the drug and for some weeks later, implying that an inflammatory exudative process had been taken care of, thereby permitting bile drainage.

I should like to ask Dr. Davidson if he thinks the initial episode of jaundice — that is, infectious hepatitis — some years before led to the condition under discussion or whether it was merely an interesting coincidence.

DR. DAVIDSON: I had hoped you would tell us that. It seems reasonable that it may have.

DR. JONES: That is what I thought in retrospect. In many of these patients, the itching occurs for many months, in this case more than a year, without any jaundice whatever, as far as the patient can tell.

DR. DAVIDSON: Is it your opinion that this was primarily an intrahepatic disease?

DR. JONES: Yes.

DR. DAVIDSON: Why did the patient get better after the T tube was put in?

DR. JONES: We have not accounted for that.

DR. DANIEL S. ELLIS: How often do you see patients with intrahepatic disease of this duration do as well as this patient did?

DR. JONES: I think the eight-year history from the beginning of the symptoms until death is unusual.

DR. TAFT: Certainly, there was no evidence at autopsy of any extrahepatic obstruction in this patient. The problem of the relation of cholesterol metabolism to this disease is unsettled in many minds. I think that Thannhauser and Magendantz[3]

probably were the first ones who emphasized this, perhaps interpreting it wrongly.

Dr. Frantz might say something regarding his studies on the subject.

DR. IVAN D. FRANTZ, JR.: I assume that the thing that Dr. Taft wants me to describe is the mechanism that causes the cholesterol to go up, and I cannot do that. So instead I shall say a few words about the changing status of our ignorance of the regulation of blood cholesterol. First, about the excretion of cholesterol: only as recently as six months ago, the picture one had to draw of the excretion or elimination of cholesterol was that some of it was oxidized, but most of it was excreted into the gastrointestinal tract, not by way of the bile but out through the intestinal mucosa. The basis of this belief was that if all the bile is allowed to drain from an animal, the animal will still excrete just as much steroid in the stools as it did before. Recently an article[11] has come out from the Chaikoff laboratory in California to the effect that this is not the true picture but that most of the cholesterol is excreted in the bile. Presumably the reason that this fact was not learned earlier is that most of the cholesterol in the bile has been partly oxidized. This material will no longer precipitate with the steroids, but appears in the saponifiable fraction, and before the use of radioactive carbon, it was missed. If we accept this recent work, we have an explanation that would apply here. We can then say that the liver was not eliminating cholesterol as it should, and that was the reason why the blood cholesterol was elevated.

The other possibility is that the liver of the person with biliary obstruction is synthesizing too much cholesterol. Evidence is now beginning to accumulate that this change occurs also and that in biliary obstruction the liver synthesizes cholesterol at too rapid a rate. We may have a double explanation for the phenomenon.

DR. JONES: Partly it would have to be caused by failure to excrete, especially when one notes the rapidity with which the cholesterol level dropped after insertion of the T tube.

DR. FRANTZ: That could be explained by the assumption that when the back pressure of bile had been relieved, the liver stopped synthesizing cholesterol too fast.

DR. EDWIN O. WHEELER: Did this patient have coronary-artery disease?

DR. JONES: No.

DR. WHEELER: It has been said that patients with this type of hypercholesterolemia do not have premature arteriosclerosis, in contrast to patients with other forms of hypercholesterolemia such as idiopathic essential hypercholesterolemia or essential hyperlipemia with secondary hypercholesterolemia.

DR. JONES: Is it not true that a careful examination was made of the coronary arteries and the aorta and that they were extraordinarily smooth?

DR. TAFT: The coronary arteries were described as having very small intimal plaques. The aorta showed but three intimal plaques in the abdominal portion. The rest of the aortic intima was smooth.

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"WE NEVER HAD IT SO GOOD"

IN somewhat more grammatical but no less material terms *Medical Economics* reports that the average physician in private practice has experienced a 35 per cent increase in his income in four years and is presently in a much better financial position than at any time in the past, with something over $15,000 per year net income before taxes. New England, which appears to be settling on education and summer visitors for its major industries, trails the rest of the country with an average medical net income of $12,158. Doctors' gold is to be found especially in the West, where the average physician's income exceeds that of his Boston homologue by $5,742. For the bright young Aesculapian to strike it rich, therefore, *Medical Economics* would guide him to a city of between 50,000 and 500,000 on the West Coast, with the promise of plenty of lettuce when he has been ten to twenty years in practice.

The best comment is not to deride or to envy but to suggest that the physician also may be a child of his economic period. Caught in the spiral of rising wages and prices, with a commanding social position in a cash culture, having forgotten the depression in learning the easier half of the Keynesian formula, he hastens on in supposedly thriftless opulence to his ultimate reward, whatever that may be. The voice of his national organization is echoed by his district local sheet. From the time of Hippocrates to that of Hess, the patient's right has been to have a personal physician whose duty it is to charge his fee for service and collect it himself. There are differences of medical opinion about how best to keep this up. The academic peerage, loaded with deficit spending to teach impecunious medical undergraduates, would like governmental help to pay for the care of teaching material and to maintain the salaries of research assistants and technicians, whereas medical entrepreneurs would prefer to run their private clinics with the least possible governmental interference.

The rapid advance of medicine as a science has been achieved by special investigators within the specialties. A truly significant contribution may require the narrow concentration of one man's best professional years. His livelihood, his tools and his patients must be supplied by an institution. Only a large private clinic or teaching hospital has the variety of clinical material from which to draw the cases of the particular disease that a specific specialist studies, diagnoses and treats. He is the medical artisan, as completely alienated from the material of his art as the machine-tool operator in a large manufacturing corporation. That this is no accident, an attentive view of history as taken by Max Weber* will show.

As the western world changed from one world family in the Middle Ages into separate groups or nations it was at the expense of the individual feudal

*Weber, M. *Essays in Sociology*. 409 pp. Translated by H. H. Gerth and C. Wright Mills. New York: Oxford University Press, 1946.

right to raise and keep an army and to control the administrative apparatus over a territory. The Renaissance brought in the ideal of the dignity and value of the individual. Modern mercantile man invented, as a countervailing power to the state, the corporation, the undying group of individuals to utilize the knowledge and skills of dying but replaceable actual individuals. Hence the current hypertrophy of the managerial or bureaucratic class in private enterprise as in government. Modern medicine has its similarity to other fields. The eminent surgeon directs his private clinic with his operating chiefs of staff, and arranges the succession. The teaching-hospital professor becomes a public figure with his academic following, a regency of trustees making the appointments. The neurosis of the physician practicing by himself is that he views with suspicion but strictly depends upon the large medical group that produces and controls the means and most of the material of his lifework.

The country never had it so good, but as medicine becomes more complex and more efficient the national medical bill will be doubled an unknown number of times. Mitigation of this perplexing situation is not far to seek and comes with the realization that the natural complexities of modern medicine and modern society alike are gradually making it increasingly logical for each doctor not to abdicate but to pool his individual rights as well as talents to do his job well. The peculiar American organizing genius is characterized not so much by elevating the best head or the best heart as by selecting the less intellectual and more realistically practical of possible choices as a top manager, by profound disrespect for bureaucrats and by the facility with which the rascals are turned out, however well entrenched. The average American doctor, like any other of his fellow citizens in the bite of personal circumstance, is an unfailing source of succour for anyone else in distress, a spirit likely to sanctify a fee, however charged, collected or allocated.

ACCIDENTAL POISONING

Few persons, including physicians (except medical examiners), realize the number of deaths caused by poisons. According to the Public Health Service 1436 deaths occurred in this country in 1948 from acute accidental poisoning (not suicidal) by solids or liquids. Barbiturates accounted for the largest number, 419, and methanol or other alcohols for 140. Many unusual agents, such as chemicals employed in therapy and in industry and for other purposes, contributed to these figures. Moore, Alexander and Ipsen* state that in Massachusetts 147 deaths were due to poisons in 1948; over a ten-year period the number of deaths per year varied from 120 to 189. Comparing the deaths in the decade 1938-1948 with similar figures for the previous ten years, the authors observe that barbiturates showed the "only significant and ominous increase in the more recent period." The deaths from barbiturates rose 4.9 times, and the suicides rose not less than 11.6 times. A long list of chemicals, therapeutic and nontherapeutic, caused the accidental deaths.

On the other hand, there were 3.8 times more deaths from the alkaloid group of sedatives in the earlier period than in the 1938-1948 group, and the cases of suicide decreased 1.8 times. This drop undoubtedly represents the rigid control to which the alkaloids are subjected and suggests the need for even more effective state or federal control of barbiturates.

Of the deaths certified by medical examiners in these last ten years poisons caused 6.6 per cent. This is not a high incidence in comparison with fatal automobile accidents. Such figures, however, should increase the respect of both the medical profession and the laity for the potential dangers of chemical agents, both therapeutic and nontherapeutic. Whether they are classed as inorganic poisons, organic poisons, composite poisons, sedatives, anesthetics, or pesticides and so forth, more effective legal control of the sale and distribution of all such agents is needed. There should be less carelessness in the handling of chemical agents and drugs in the home, hospital, industry and on the farm. Extreme caution should be exercised when these agents are left exposed to children and to adults who are unfamiliar with their possible dangers. Physicians are accustomed to the careful examination of sick people and to the deliberation of the

*Moore, M., Alexander, L., and Ipsen, J., Jr. Deaths from poisoning: Massachusetts, 1938-1948. *New Eng. J. Med.* 246:46-52, 1952.

proper dosage of drugs for the patient, but extra precautions in the use of agents that have possibly unfavorable side reactions are needed. The barbiturates are the prime problem of the day and deserve the most careful consideration of physicians, legal authorities and the public.

EASTER SEALS

The Bay State Society for the Crippled and Handicapped opens the annual Easter Seal campaign with a word of thanks for the generous response to the 1952 appeal, which represented the largest amount raised during the history of the organization. The Society was able to expand its efforts to make rehabilitation services available to an increasing number of handicapped people. During the year ending September, 1952, such services were provided for a total of 2338 persons in need of them, and advice and information were given to 989 others. Of the patients receiving direct aid, 1839 were children.

The work of the Society in the areas of Boston, Worcester and the western section of the Commonwealth has meant the difference between independence and helplessness for many persons. Thus, the Boston Clinic, during the first fifteen months of operation, discharged 223 patients to a new, useful way of living (48 were returned to gainful employment). The rehabilitation centers in Worcester and the western area made similar progress. Not the least valuable of the Society's many services is the provision of summer-camp vacations for a number of handicapped children.

To continue its valuable work, the Bay State Society for the Crippled and Handicapped must meet with another generous response to its appeal. It is hoped that doctors will be in the vanguard of those who contribute to the Easter Seal campaign, which is practically the only source of income for the Society.

PART-TIME INDUSTRIAL MEDICINE

Since the time of Ramazzini, the father of industrial medicine, whose contribution to this specialty will be the subject of comment at a later date, the medicine of factory and of foundry, of mine and of mill, has assumed a position of increasing importance in an increasingly mechanized society. Whereas industry in medicine has always been an indispensable prerequisite of professional success, medicine in industry now provides another avenue into which physicians may direct their own industrious efforts.

Recognizing the rapid development during the past decade of in-plant employee health programs by American industry, medical schools have been including lectures on the subject in their undergraduate curriculums, and graduate schools of medicine and public health have been constructing postgraduate courses of training. Many physicians who have lacked such orientation, however, are being asked to go into industries in their communities to build part-time employee health services, and the American Academy of General Practice, quick to appreciate the need, has expressed the desire that its members might be given the opportunity of learning some of the special aspects of this growing field.

To meet this apparent need a two-day pilot seminar will be held early next month at the Harvard School of Public Health. The seminar will be jointly sponsored by the School of Public Health, the Academy of General Practice, the Council on Industrial Health of the American Medical Association and the Liberty Mutual Insurance Companies, and will count as credits toward the postgraduate study hours required by the Academy.

The seminar will be divided into four half-day sessions. The first will be on industrial injuries, with emphasis on compensation laws, claims handling and safety. The second will deal with occupational diseases, particularly regarding problems of diagnosis and of evaluating the severity of a toxic exposure. At the third, industrial medical practice, including its aims and scope, its industrial relations aspects and its relations to private practice, will be the subject, and the fourth will consist of a discussion of the role of industrial medicine in the country's problems of medical care.

Another illustration is thus made available of the way in which the general practitioner must continue to be the minute man of the profession. Not himself a specialist, he must nevertheless be prepared to hold the outposts of all the specialties.

Massachusetts Register. — *Occasionally it happens that intelligence of common interest to business people, among whom physicians are invariably to be numbered, may be propagated through the pages of this Journal without having the exclusive odor of medicine.*

Boston M. & S. J., *March 30, 1853*

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

BARRON — David Barron, M.D., of Brockton, died on March 4. He was in his fifty-sixth year.

Dr. Warren received his degree from Tufts College Medical School in 1921. He was formerly city health officer and was a member of the staff of Brockton Hospital.

He is survived by two daughters, two brothers and two sisters.

CHASE — Henry M. Chase, M.D., of Boston, died on February 15. He was in his seventy-ninth year.

Dr. Chase received his degree from Harvard Medical School in 1901. He was a member of the American Urological Association and a fellow of the American College of Surgeons and American Medical Association.

He is survived by his widow.

DOTEN — Arthur C. Doten, M.D., of Worcester, died on March 3. He was in his seventy-seventh year.

Dr. Doten received his degree from Long Island College of Medicine in 1899. He was formerly surgeon to the Worcester Police Department.

He is survived by his widow, a stepdaughter and a brother.

STODDARD — Mortimer J. Stoddard, M.D., of Springfield, died on February 22. He was in his seventy-ninth year.

Dr. Stoddard received his degree from University of Vermont College of Medicine in 1898. He was formerly president of the Springfield Hospital staff and visiting physician at the hospital and a fellow of the American Medical Association.

He is survived by a daughter, two grandchildren and a sister.

BOSTON MEDICAL LIBRARY

TUFTS MEDICAL ALUMNI BULLETIN

The Library is in receipt of a bound volume containing the issues of the *Tufts Medical Alumni Bulletin* for the first ten years from its inception in 1942. It is the gift of Dr. Harry Blotner, the editor.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

LIST OF REPORTABLE DISEASES

A few changes have been made in the list of diseases that physicians and householders are required by law to report to local boards of health. Weil's disease will hereafter be reportable under "Leptospirosis," so that infections due to *Leptospira canicola, Lept. pomona* and *Lept. icterohaemorrhagiae* can be included. Salmonella carriers have also been added to the list. The other changes largely involved terminology. Copies printed on cards are available on request.

The present list is as follows:

I. REPORTABLE TO LOCAL BOARD OF HEALTH:*

- Actinomycosis
- Anthrax
- Asiatic cholera
- Chicken pox
- Diphtheria
- Dog bite
- Dysentery:
  - a. Amebic
  - b. Bacillary
- Encephalitis, infectious
- German measles
- Glanders
- Hepatitis, infectious
- Leprosy
- Leptospirosis, (including Weil's disease and other infections due to leptospira)
- Lymphocytic choriomeningitis
- Malaria
- Measles
- Meningitis:
  - a. Meningococcal
  - b. Other: Pfeiffer bacillus
    pneumococcal
    streptococcal and so forth
- Mumps
- Ophthalmia neonatorum
- Plague
- Poliomyelitis:
  - a. Paralytic
  - b. Nonparalytic
- Psittacosis
- Rabies
- Rocky Mountain spotted fever
- Salmonellosis
  (Paratyphoid infections)
- Salmonella carrier
- Scarlet fever (including streptococcal sore throat)
- Smallpox
- Tetanus
- Trachoma
- Trichinosis
- Tuberculosis (all forms)
- Tularemia
- Typhoid fever
- Typhoid carrier (including cholecystitis of typhoid origin)
- Typhus fever
- Undulant fever
- Whooping cough
- Yellow fever

II. REPORTABLE DIRECTLY TO MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH:

- Chancroid
- Gonorrhea
- Granuloma inguinale
- Lymphogranuloma venereum
- Syphilis

*Diseases declared by the Department of Public Health to be dangerous to the Public Health and reportable under the authority of Section 6 of Chapter 111 of the *General Laws*, appearing in the Tercentenary Edition thereof, as amended by Chapter 129 of the *Acts* of 1948.

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR FEBRUARY, 1953

Résumé

Disease	February 1953	February 1952	Seven-Year Median
Chancroid	3	2	2
Chicken pox	4228	2040	2044
Diphtheria	0	3	19
Dog bite	523	611	583
Dysentery, bacillary	18	0	6
Encephalitis, infectious	1	7	2
German measles	298	1124	143
Gonorrhea	182	197	197
Granuloma inguinale	0	1	0
Hepatitis, infectious	83	10	6*
Lymphogranuloma venereum	2	0	1
Malaria	0	1	1
Measles	220	12,993	2021
Meningitis, meningococcal	4	5	7
Meningitis, Pfeiffer bacillus	2	4	4
Meningitis, pneumococcal	2	3	4
Meningitis, staphylococcal	0	0	0
Meningitis, streptococcal	0	0	0
Meningitis, undetermined	7	8	5
Mumps	1023	1710	1301
Poliomyelitis	0	1	1
Salmonellosis	11	8	4
Scarlet fever	630†	394	627
Syphilis	79	216	198
Trichinosis	1	0	1
Tuberculosis, pulmonary	177	174	189
Tuberculosis, other forms	6	13	11
Typhoid fever	1	0	0
Undulant fever	2	1	2
Whooping cough	109	269	294

*Four-year median.

†Includes streptococcal sore throat.

Comment

Diseases above the seven-year median included chicken pox, bacillary dysentery, German measles and salmonellosis.

For the seventh consecutive month, the number of cases of chicken pox exceeded the number in the corresponding month of the previous year. (The peak is usually reached in March, but occasionally comes in April or May.)

The 298 cases of German measles were above the seven-year median but much below February, 1952 (1124 cases).

The incidence of salmonellosis has been above that of the previous year every month but one since May, 1952.

The diseases below the seven-year median were diphtheria, measles, meningitis and whooping cough.

In six of the last eight months, no cases of diphtheria have been reported. Only 3 cases have been discovered since July 1, 1952 — 2 in December and 1 in January.

The low level of measles is to be expected, since 1952 made the highest record in the history of the State. The 220 cases set the lowest record ever made for February.

Whooping cough has been making new low records each month since June, 1952.

Geographical Distribution of Certain Diseases

The following diseases were reported from the communities named:

Dysentery, bacillary: Boston, 2; Danvers, 4; Grafton, 1; Newton, 2; Rockland, 1; Williamsburg, 1; Worcester, 1; Wrentham, 6; total, 18.

Encephalitis, infectious: Northboro, 1.

Hepatitis, infectious: Boston, 14; Cambridge, 4; Charlton, 1; Fall River, 1; Falmouth, 1; Fort Devens, 2; Holden, 2; Hingham, 1; Leominster, 3; Malden, 1; Marlboro, 1; Middleboro, 1; Millbury, 11; Milton, 1; Needham, 1; Springfield, 3; Sturbridge, 1; Worcester, 29; Wrentham, 5; total, 83.

Lymphocytic choriomeningitis: Cambridge, 1.

Meningitis, meningococcal: Fall River, 1; Holyoke, 1; Springfield, 1; Winchendon, 1; total, 4.

Meningitis, Pfeiffer bacillus: Lowell, 1; Swampscott, 1; total, 2.

Meningitis, pneumococcal: Boston, 1; Worcester, 1; total, 2.

Meningitis, undetermined: Ayer, 1; Barnstable, 1; Beverly, 1; Chatham, 1; New Bedford, 1; Somerville, 1; Worcester, 1; total, 7.

Salmonellosis: Boston, 2; Fitchburg, 1; Littleton, 1; Malden, 1; Methuen, 1; Milton, 1; Natick, 1; Worcester, 3; total, 11.

Tetanus: Arlington, 1.

Trichinosis: Cambridge, 1.

Typhoid fever: Boston, 1.

Undulant fever: Methuen, 1; Westminster, 1; total, 2.

CORRESPONDENCE

REVOCATION OF LICENSE

To the Editor: At the meeting of the Board of Registration in Medicine held February 19, it was voted to revoke the registration of Dr. Leo J. Mandeville, formerly of 5 Taylor Street, Holyoke.

Robert C. Cochrane, M.D.
Secretary

State House
Boston

TECHNIC OF TRANSDUODENAL SPHINCTEROTOMY

To the Editor: I found the article entitled "Transduodenal Sphincterotomy for Chronic Relapsing Pancreatitis" by Major and Ottenheimer, in the January 22 issue of the *Journal*, very interesting. Under "technic" the authors state that "the gall bladder should always be removed if the sphincter is to be cut." Do they always consider the gall bladder diseased in these cases or do they think that interfering with the physiology of the sphincter is apt to produce stones in the gall bladder later on?

Also, I cannot help asking if "MacBurney" is now the preferential spelling in New England. This was written through an amanuensis and not with a quill pen. Silly, isn't it?

David Metheny, M.D.

Seattle, Washington

Dr. Metheny's letter was submitted to Dr. Major, whose reply is as follows:

To the Editor: As pointed out by Doubilet and Mulholland, in their study entitled "Etiology and Treatment of Pancreatitis" (*New York State J. Med.* 49:2938-2944, 1949), cholecystectomy at the time of sphincterotomy, without apparent gall-bladder disease, is indicated for two reasons: being a muscular organ, under proper stimulation the gall bladder can be the cause of elevated pressure in the common bile duct, possibly increasing the chance of reflux in the pancreatic duct; and the gall bladder is a concentrator of bile, and since it has been shown that the more concentrated the bile, the more severe the reaction when reflux into the pancreatic duct occurs, cholecystectomy eliminates the concentrating factor.

James W. Major, M.D.

Willimantic, Connecticut

QUO VADIMUS?

To the Editor: Quo vadimus? For Americans that happens to be the question of the day. For members of the profession closest to mankind it is the question of the hour.

According to an intelligent colleague who was educated and trained largely abroad, the traditional propensity of medical practitioners in France is to depreciate the science and of those in Germany to depreciate the art of medicine but of those in England to do neither — there, a happy mean of those elements is maintained. But here doctors are scurrying to outrun the Germans on an inhumanistic, ultrascientific course. This will doom medicine as a learned profession and change it into a business enterprise.

Wanton specialization constitutes a dangerous abuse of the economic principle of the division of labor, which has consistently resulted in the increased cost of the services of members of both trades and professions. The optimal proportion of special to general practitioners has already been passed in most specialties, this superabundance engendering a new breed of specialists, long on theory and short on practice, slighting the simpler clinical studies and resorting to the more costly aids and procedures. Only men with a professional attitude as well as an aptitude can provide adequate medical care, which presupposes a personal humanistic service independent of the patient's sociologic status and dependent on his individual demands. To meet such requisitions the medical student should be trained in the art of medicine with more practice and less theory. Premedical subjects should be broad enough to furnish a knowledge of man and his environments, past as well as present. To qualify even for premedical studies all candidates should be re-

quired to pass a test to determine not only their intelligence quotient but also their morality quotient. It would surely be less difficult to weed out prospective medical students unfit for the implicit trust imparted to physicians than to eliminate unethical established practitioners, many of whom are ensconced in reputable societies in roles like that of Dr. Jekyll and Mr. Hyde.

G. W. HAIGH, M.D.

Worcester, Massachusetts

ANNUAL REGISTRATION

To the Editor: It is highly unlikely that annual registration of physicians will improve the quality of medical care. I wish to express strong opposition to House Document No. 158.

DWIGHT M. FOWLER, M.D.

Duxbury, Massachusetts

REMUNERATION OF SCHOOL PHYSICIANS

To the Editor: At a meeting of the Massachusetts School Physicians' Association it was recently unanimously voted to accept the resolution presented by a special committee, appointed last January, "That the minimum salary of a school physician be based on $10.00 per hour."

The committee consisted of Dr. George S. Rust, of Gloucester, Dr. Frederick Paul, of Newtonville, Dr. Edward Rosen, of Revere, Dr. Francis C. Buckley, of Foxboro, Dr. S. Edward Chalfen, of Cambridge, Dr. E. L. Eldredge, of Hingham, Dr. Sidney S. Listernick (chairman), of Everett, and Dr. Francis F. Cary (president), of Greenfield, *ex-officio* member.

SIDNEY S. LISTERNICK, M.D., *Secretary*
Massachusetts School Physicians' Association

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Essentials of Public Health. By William P. Shepard, M.D., M.A. With the collaboration of Charles E. Smith, M.D., D.P.H., Rodney R. Beard, M.D., M.P.H., and Leon B. Reynolds, Sc.D. With a foreword by Ray L. Wilbur, M.D., LL.D., Sc.D., chancellor, Stanford University. Second edition. 12°, cloth, 581 pp., with 20 illustrations, 27 charts and 22 tables. Philadelphia: J. B. Lippincott Company, 1952. $6.50.

The first edition of this manual was published in 1948. This new edition has been revised to include new material, and the tables, charts and figures have been brought up to date. A chapter has been added on the physician and the public-health nurse. The chapters comprise the relation of the practicing physician to public health, environmental sanitation (water, sewage, refuse, food hygiene, insect and communicable disease and the control of tuberculosis and venereal diseases), general public-health problems (maternal and child health, heart disease, cancer and so forth), school health services, health education, industrial hygiene, light, heat and ventilation, statistics and public-health nursing. Lists of references are appended to the different chapters. There is a good index, and the publishing is excellent. The various aspects of public health are well summarized.

Gesundheitspolitik: Reds. Gehalten auf der Konferenz der Gesundheitsminister in Düsseldorf, Am 13. Februar 1952. By ministerial councilor Dr. Med. Habil. Otto Buurman, Hannover. 8°, paper, 58 pp., with 24 illustrations. Stuttgart: Georg Thieme, 1952. Kart. DM 5.85. (Distributed by Grune and Stratton, New York.)

This lecture on public health and its relation to government is based on statistics for Germany. Numerous comparative charts and tables with descriptive text comprise the first part of the book. The last part is devoted to a comprehensive summary of the various problems of public health in Germany.

The Advance to Social Medicine. By René Sand. 8°, cloth, 655 pp. New York: Staples Press, Incorporated, 1952. $8.50.

Dr. Sand is professor of social medicine in the University of Brussels, Belgium. His book constitutes a comprehensive history of social medicine in all its aspects. The various chapters discuss the history of medicine in a social sense, the history of hospitals, personal hygiene, public health, social hygiene, industrial medicine, social assistance and of the studies of man. The final chapter, entitled "The Advent of Social Medicine," portrays the present status in all countries of the world, including the United States and Canada, and gives a discussion of social medicine in general. There is a 9-page bibliography and indexes of subjects and personal names. The publishing is excellent. The book is recommended for all libraries, medical and general.

Ansprachen. By Professor Dr. H. C. Walter Stoeckel, privy councilor for health. 8°, paper, 133 pp. Stuttgart: Georg Thieme, 1952. Kart. DM 7.80. (Distributed by Grune and Stratton, New York.)

This volume brings together eleven addresses by the well known German gynecologist, Walter Stoeckel. They include two delivered upon his eightieth birthday, March 14, 1951, at a celebration held in his honor. The small volume is a valuable addition to the history of gynecology.

Surgery of the Chest: A handbook of operative surgery. By Julian Johnson, M.D., D.Sc. (med.), professor of surgery, University of Pennsylvania School of Medicine and Graduate School of Medicine; and Charles K. Kirby, M.D., assistant professor of surgery, University of Pennsylvania School of Medicine. 8°, cloth, 387 pp., with 81 illustrations by Edna Hill. Chicago: Year Book Publishers, Incorporated, 1952. $9.00.

This book is an atlas depicting the operations on the chest and its organs with descriptive text. General principles are discussed, followed by chapters on the surgery of the lungs, the esophagus, heart and great blood vessels, pulmonary tuberculosis and miscellaneous operations (for diaphragmatic hernia, correction of pectus excavatum and mediastinal tumors). The plates show the step-by-step procedures for the various operations that they have found reliable. There is a good index, and the publishing is excellent.

Principles, Problems, and Practices of Anesthesia for Thorac.. Surgery. By Henry K. Beecher, M.D., Henry Isaiah Dorr Professor of Research in Anesthesia, Harvard Medical School, and director, Department of Anesthesia, Massachusetts General Hospital. 8°, cloth, 65 pp., with 2 illustrations. Springfield, Illinois: Charles C Thomas, 1952. $2.50. (Publication No. 139, *American Lecture Series.*)

The author briefly covers anesthesia in thoracic surgery. Most of the problems encountered in all intrathoracic surgery are met with in lobectomy or pneumonectomy, and these operations are discussed in detail, including equipment, premedication, choice of anesthetic and procedures at the end of operation. There are also a chapter on special problems with infants and small children and brief discussions of transthoracic operations on the heart and great blood vessels, thymectomy for myasthenia gravis, esophagectomy and gastrectomy, drainage of lung abscess and thoracoplasty.

Anurie bei Chromoproteinurie (Hämolysenniere, Crush-Niere). By Professor Dr. Hans U. Zollinger. 8°, paper, 138 pp., with 42 illustrations. Stuttgart: Georg Thieme, 1952. Kart. DM 14.70. (Distributed by Grune and Stratton, New York.)

This small monograph presents a comprehensive survey of the literature of acute insufficiency of the kidney due to hemolysis and myolysis. The subject is divided into seven parts. The first, which discusses the causative factors, is based on 50 cases found in 17,000 autopsies performed during the past ten years. The other chapters deal with the clinical aspects, autopsy findings, pathogenesis, relation between anatomic variations of the kidney and clinical symptoms, nomenclature and treatment. A bibliography of 486 titles is appended to the text. The monograph is a valuable reference work and should be in all medical reference collections.

Advances in Medicine and Surgery: From the Graduate School of Medicine of the University of Pennsylvania. 8°, cloth, 441 pp., with 43 illustrations. Philadelphia: W. B. Saunders Company, 1952. $8.00.

The papers contained in this volume were read during a postgraduate course given at the University of Pennsylvania in 1950. They comprise a series of symposia, including the present status of adrenocortical hormones, the role of potassium in health and disease, hypertension (newer aspects of medical and surgical treatment, newer concepts in preoperative evaluation and preparation of patients), thromboembolism, pulmonary infections, relief of pain, current status of the cancer problem, recent developments in viral diseases and functional disorders (psychosomatic, gastrointestinal, neurologic, cardiac and dermatologic). Fifty-five Philadelphia physicians took part in the course. There is a good index of subjects, and the publishing is excellent. The book is important as a periodical volume and should be in all medical libraries.

Expert Committee on Environmental Sanitation. Second Report. 8°, paper, 21 pp. Geneva: World Health Organization, 1952. 1/3 $0.15; Sw.fr. 0.60. (*World Health Organization, Technical Report Series No. 47.*)

In this second report the committee recommends that regional centers, offering field training facilities, should be established for the postgraduate training of sanitary engineers and medical officers of health, that urban centers providing training in inspection duties should be set up, and that demonstration training centers should be inaugurated in rural areas to educate voluntary workers.

Expert Committee on Maternity Care. First Report. A Preliminary Survey. 8°, paper, 23 pp. Geneva: World Health Organization, 1952. 1/3 $0.15; Sw.fr. 0.60. (*World Health Organization, Technical Report Series No. 51.*)

In this preliminary report, in which the committee compared the women of the Eastern countries with those of the West, noting the ease of deliveries in the East and the difficulty that the women of the West sometimes experience, optimum standards are set up for prenatal, hospital and postnatal care. Other topics discussed include training of personnel, evaluation of a maternity-care program and the role of the physician, the midwife, the nurse and home help.

Advances in Pediatrics. Vol. V. Editor, S. Z. Levine, M.D., Cornell University Medical College, New York. 8°, cloth, 273 pp., with illustrations and tables. Chicago: Year Book Publishers, Incorporated, 1952. $7.00.

The contents of this fifth volume in a standard series includes summaries of the recent literature on the treatment of bacterial meningitis, the nephrotic syndrome, the relation of vitamin K deficiency to hemorrhagic disease of the newborn, angiocardiographic studies in children, iron metabolism and BCG vaccination. Bibliographies are appended to the chapters, and there are indexes of subjects and authors.

Congenital Dysplasia of the Hip Joint and Sequelae (in the Newborn and Early Postnatal Life.) By Vernon L. Hart, M.D., assistant professor of surgery, University of Minnesota Medical School. 8°, cloth, 187 pp., with 83 illustrations. Springfield, Illinois: Charles C Thomas, 1952. $5.00. (Publication No. 102, *American Lecture Series.* The Detroit Orthopaedic Lecture, presented under the auspices of the Wayne County Medical Society, Detroit, December 6, 1948.)

Dr. Hart discusses his subject in all its aspects from etiology to treatment. The literature is surveyed, and there is a bibliography of 141 titles. The monograph is well illustrated. It should be in all orthopedic collections.

Diseases of the Nose, Throat and Ear: A handbook for students and practitioners. By I. Simson Hall, M.B., Ch.B., F.R.C.P.E., F.R.C.S.E., surgeon to the Royal Infirmary, Edinburgh (Department for Diseases of Nose, Throat and Ear), and lecturer in diseases of nose, throat and ear, University of Edinburgh. Fifth edition. 12°, cloth, 463 pp., with 82 illustrations and 8 colored plates. Baltimore: Williams and Wilkins, 1952. $4.00.

The first edition of this manual was published in 1937. In this fifth edition, the format has been retained, and material on treatment has been added where appropriate. The author has refrained from discussing controversial matters. There is a good index. The printing was done in Great Britain. The need for five editions in fifteen years speaks well for the popularity of the small book.

Kwashiorkor in Africa. By J. F. Brock, D.M., F.R.C.P., professor of the practice of medicine, University of Cape Town, Union of South Africa, and consultant in nutrition, World Health Organization; and M. Autret, Dr. Pharm., chief, area and field branch, Nutrition Division, Food and Agriculture Organization of the United States. 8°, paper, 78 pp., with 11 illustrations and 5 tables. Geneva: World Health Organization, 1952. 5/ $1.00, Sw. fr. 4. (*World Health Organization Monograph Series No. 8.*)

Kwashiorkor is indigenous to Africa and is described as a dietary deficiency disease. The authors present the facts and findings of a survey made in central and tropical Africa during the last three months of 1950. The medical aspects, diet, etiology and prevention of the disease are discussed in detail. A list of 75 references concludes the text.

Vascular Diseases in Clinical Practice. By Irving S. Wright, M.D., professor of clinical medicine, Cornell University Medical College, and attending physician, New York Hospital. Second edition. Chicago: Year Book Publishers, Incorporated, 1952. $8.50.

Four years have elapsed since the publication of the first edition of this book, and the author has taken advantage of the opportunity to revise and augment his text. Material on atherosclerosis, shoulder girdle syndrome, cryoglobulinemia and the cold agglutinins, anticoagulant therapy and new drugs has been added. A chapter on the responsibility of the physician to the patient before and after amputation has also been added. Short lists of references are appended to the chapters, and there is a good index.

Medical Biographies: The ailments of thirty-three famous persons. By Philip M. Dale, M.D. 8°, cloth, 259 pp., with 32 portraits. Norman: University of Oklahoma Press, 1952. $4.00.

These biographies of famous persons who were afflicted with disease or bodily ailments begin with Buddha, 563-483, B.C., and Charlemagne, 742?-814, A.D., and Robert Louis Stevenson, 1850-1894. The list comprises 5 presidents of the United States: George Washington (1732-1799), Andrew Jackson (1767-1845), James A. Garfield (1831-1881), Grover Cleveland (1837-1908) and William McKinley (1843-1901). Garfield and McKinley were assassinated, and Jackson was injured in a gun episode. President Lincoln is not included in the biographies, but his mother, Nancy Hanks Lincoln, takes his place. The selection of persons is excellent; the scientists include a physician who is little known in that capacity: Jean Paul Marat (1743-1793) was a physician of note but is famed as a ruthless leader of the French revolution and the victim of Charlotte Corday. Other scientists are Sir Isaac Newton (1642-1727), Immanuel Kant (1724-1804) and Charles Darwin (1809-1882). There are portraits of 32 of the subjects (no portrait of Mrs. Lincoln exists). A bibliography of sources is appended to the text, which is written in an easy style. The book is recommended for all collections of medical and general history collections.

Clinical Applications of Recreational Therapy. By John E. Davis, Sc.D., chief of corrective therapy, United States Veterans Administration, Washington, D. C. 8°, cloth, 118 pp., with 21 illustrations. Springfield, Illinois: Charles C Thomas, 1952. $3.75. (Publication No. 123, *American Lecture Series.*)

Dr. Davis discusses the remedial use of play in mental disorders. There are two chapters on the patient who has been subjected to prefrontal lobotomy. The appropriate literature is covered, and there is a bibliography of ninety-five items.

NOTICES

SEMINAR ON INDUSTRIAL HEALTH

A two-day seminar on part-time employee health services in industry will be held at the Harvard School of Public Health on April 3 and 4.

The seminar has been accepted for credits toward the postgraduate study hours required for continued membership in the American Academy of General Practice.

Further information may be obtained from the Secretary, Harvard School of Public Health, 55 Shattuck Street, Boston 15, Massachusetts.

BOSTON CITY HOSPITAL ALUMNI ASSOCIATION

Clinical meetings of the Boston City Hospital Alumni Association will be held in the Hospital on Saturday, April 25, at 9:20 a.m. The medical program will be presented in the Cheever Amphitheater, with Dr. William B. Castle as moderator, the surgical program in the Amphitheater of the Mallory Institute of Pathology, with Dr. A. J. A. Campbell as moderator, and the orthopedic program in the Shortell Unit, with Dr. Robert T. Rix, as moderator.

SOUTH END MEDICAL CLUB

The regular luncheon meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, April 21, at 12 noon.

The guest speaker will be Ernest M. Daland, M.D., chief of staff, Pondville State Cancer Hospital and a member of the Board of Consultation, Massachusetts General Hospital. His subject will be "Cancer Detection in the Physician's Office."

All physicians are cordially invited to attend.

SOCIETY FOR INVESTIGATIVE DERMATOLOGY, INC.

The Society for Investigative Dermatology, Incorporated, will hold its fourteenth annual meeting at Hotel Belmont Plaza, New York City, May 30 and 31.

AMERICAN COLLEGE OF ALLERGISTS

The annual conclave of the American College of Allergists will be held at the Conrad Hilton Hotel, Chicago, April 24-29. The first four days will be devoted to instruction under the tutelage of recognized authorities and the last three to a discussion and reporting of recent advances in the field of allergy by the investigators themselves. Detailed information may be obtained from the American College of Allergists, La Salle Medical Building, Minneapolis 2, Minnesota.

SOCIETY MEETINGS AND CONFERENCES

April 1-27. Consultation Clinics for Crippled Children in Massachusetts. Page 523, issue of March 19.

April 3 and 4. Seminar on Industrial Health. Notice above.

April 4. Problems in Hematology. Drs. William B. Castle and Frank Gardner. Mount Auburn Hospital, Cambridge. 10:05 a.m.

April 6-10. Federation of American Societies for Experimental Biology. Page 526, issue of March 19.

April 6 and 20. Hartford Medical Society. Page 42, issue of January 1.

April 6-May 4. Massachusetts Department of Mental Health. Postgraduate Seminar in Neurology and Psychiatry. Page 540, issue of October 2.

April 8. Postgraduate Medical Institute. Boston. Page 452, issue of September 18.

April 10. New England Society of Anesthesiologists. Page 395, issue of February 26.

April 10-12. American Association of the History of Medicine. Page 308, issue of February 12.

April 14. New York Society for Circulatory Diseases and New York Cardiological Society. Page 526, issue of March 19.

April 15. Tufts Medical Alumni Association. Page 525, issue of March 19.

April 15. Massachusetts Academy of General Practice. Page 480, issue of March 12.

April 16-18. Postgraduate Course in Obstetrics and Pediatrics. Page 525, issue of March 19.

April 19-24. National Industrial Health Conference. Page 308, issue of February 12.

April 21. South End Medical Club. Notice above.

April 24-29. American College of Allergists. Notice above.

April 25. Boston City Hospital Alumni Association. Notice above.

April 25. Alumni Association of the State University College of Medicine at New York City. Page 396, issue of February 26.

April 25. Graduate Club of Boston. Phi Delta Epsilon Medical Fraternity. Page 307, issue of February 12.

April 29 and October 28. New England Obstetrical and Gynecological Society. Page 868, issue of November 27.

May 7-9. American Goiter Association. Page 480, issue of March 12.

May 11-13. Aero Medical Association. Page 526, issue of March 19.

May 19-21. Massachusetts Medical Society. Hotel Statler, Boston.

May 25-31. First World Congress on Fertility and Sterility. Page 1001, issue of December 18.

May 30. Society for Investigative Dermatology, Inc. Notice above.

June 7-9. American College of Cardiology. Page 395, issue of February 26.

June 28-July 2. American Society of X-Ray Technicians. Page 480, issue of March 12.

District Medical Societies

ESSEX NORTH

May 13. Andover Country Club, Shawsheen.

WORCESTER

May 6. Annual Meeting. Sheraton Hotel. Dr. Louis H. Bauer, President, American Medical Association.

Calendar of Boston District for the Week Beginning Thursday, April 2

Thursday, April 2

*8:30-10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*9:00-10:00 a.m. Cardiac Grand Rounds. Main Amphitheater, Children's Medical Center.
9:00-10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.
*11:00 a.m.-12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.
*5:00-6:00 p.m. Surgical Division Meeting. Mount Auburn Hospital, Cambridge.

Friday, April 3

Seminar on Industrial Health. Harvard School of Public Health. 55 Shattuck Street.
*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.
*10:00 a.m.-1:00 p.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
*10:30-11:15 a.m. Diabetes Lecture. Dr. Elliott Joslin. New England Deaconess Hospital.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.
*4:00-10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Waltham Street.

Saturday, April 4

Seminar on Industrial Health. Harvard School of Public Health, 55 Shattuck Street.
*9:00 a.m. Proctology Clinic. Peter Bent Brigham Hospital.
*9:00 a.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*11:00 a.m.-12:00 m. Blood Clinic. Dr. William Dameshek. Stearns Auditorium, New England Center Hospital.

Monday, April 6

8:00-9:00 a.m. Combined Medical and Surgical Rounds for Diabetic Surgery Cases. New England Deaconess Hospital.
*8:30-9:30 a.m. Clinic by entire Surgical Staff and Anesthesia Staffs. Cheever Amphitheater, Dowling Building, Boston City Hospital.
12:00 m. Clinicopathological Conference (Boston Floating Hospital). Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*12:15-1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.
*2:00-8:30 p.m. Postgraduate Seminar in Neurology and Psychiatry. Metropolitan State Hospital, Waltham.
*7:00-9:00 p.m. Anesthesia Teaching Conference. Stearns Auditorium, New England Center Hospital.

Tuesday, April 7

*9:00 a.m. Geriatrics Clinic. Peter Bent Brigham Hospital.
11:00 a.m.-12:00 m. Regular Grand Rounds of the Pediatric Department. Dowling Amphitheater, Boston City Hospital.
*12:00 m.-1:00 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.

(*Notices concluded on page xi*)